Adherence in HIV-Positive Women Entering Antenatal Care on Antiretroviral Therapy: A Cross-sectional Study

Manuscript for dissertation requirement for a Master's of Public Health

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Submitted in fulfillment of the requirements for the degree

MASTER OF PUBLIC HEALTH

In the

SCHOOL OF PUBLIC HEALTH AND FAMILY MEDICINE

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June 2015

Plagiarism Declaration

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Dedication Page

For Mel, who I hope would be proud.

Abstract

Proper implementation of and adherence to antiretroviral therapy (ART) is significantly associated with better health and longer life in HIV-positive individuals. Consistent, adequate adherence has been shown to lead to a suppressed viral load. A low viral load delays the virus's progression and leads to better health outcomes for the individual.

Adequate adherence is especially important among HIV-positive pregnant women. How well a woman adheres to her ART can not only improve her health during pregnancy but can protect the infant from HIV by preventing *in utero* transmission of the virus. Continuing ART protects against transmission via breastmilk later in the infant's life.

While the benefits of good adherence are undeniable, the definition of adequate adherence varies widely in the literature. Taking 80 to 100 % of pills as prescribed is commonly used as the threshold for adequate adherence levels. Various methods exist for measuring ART adherence, and while some are more reliable than others, there is no gold standard.

This ambiguity in ART research extends to pregnant women, with even less known about HIV-infected women established already on ART who then become pregnant. Changes in treatment protocols in the Western Cape and improvement of ART delivery throughout South Africa have resulted in this group of long-term users growing in size. Without more research into the barriers of ART adherence in these women, efforts to scale up treatment programs and to end mother to child transmission of HIV will ultimately fail. This dissertation is an exploration of these ideas. It begins to fill the gap in current knowledge related to ART compliance in pregnant women, and gives new insights into how specific barriers to adherence can adversely affect this specific group of established ART users.

Part A is a research proposal. It presents an analysis of data collected from Phase 1 of the Maternal and Child Health Antiretroviral Treatment study (MCH-ART). This phase, with participant enrolment from April 2013 through May 2014, was a cross-sectional survey of women attending their first visit at a midwife obstetric unit in Gugulethu, Western Cape. The protocol proposes an analysis of a subgroup of this sample, consisting of 486 women who initiated ART prior to their current pregnancy. Included in this section is also a weighing of the possible benefits, harms and ethical issues with this secondary analysis.

Part B is a review of the literature, examining issues around adherence to ART. Special attention is given to studies that include pregnant women and women who are long-time users of ART. This literature review serves to explain the issues around defining adherence in research; to explore various methods of measuring adherence and their reliability; and to identify and give some background on potential risk factors measured in the MCH-ART study for poor adherence to ART in pregnancy.

Part C is the research article, which is made up of four sections: background, methods, results and discussion. This article features a quantitative analysis of the data described in Part A, with univariate and bivariate descriptions of the population. Reliability of various self-reported measures of adherence is explored to validate the chosen self-reported adherence measure. Cronbach's alphas are generated for the scale measures used in Phase 1 to assess their validity and reliability in this population. Finally a model that describes the barriers to adherence among this important group of women is built using variables identified in Part B as potential risk factors for poor adherence.

Part D consists of the appendices for the previous three sections. It includes a study approval letter form the University of Cape Town's Human Research Ethics Committee; copies of the measurement tools used in the study in English and isiXhosa; consent forms; additional inserts, including an expanded table of Cronbach's alphas and a correlation matrix; and journal submission guidelines.

Acknowledgements

Thank you very much to Professor Landon Myer for the opportunity to work with these data. I greatly appreciate the patience you showed every time you found me sitting outside your office with Stata pulled up on my laptop, for taking my questions with good humour and for the wisdom you imparted to me.

Thank you to Tammy Phillips and the MCH-ART study staff. I am so grateful for all that you have done, and I can only hope that this paper does justice to your hard work.

Thank you to Molly Bernstein and Jessica Barker. You are both the most amazing people and I cannot tell you how thankful I am to call you friends. Molly, thank you for the comments you've given me on my drafts of this work and always being kind even when it was a mess. Jess, thank you for always having an eye on what is ahead and keeping me motivated. I would never have made it out of Cape Town alive had it not been for you two.

Thank you to my family. Becky O'Sullivan, thank you for editing this work and for always understanding my craziness. Jean O'Sullivan, you are an incredibly strong woman, loving mother and a dedicated nurse. I love you very much mom, and I am eternally grateful that I take after your side of the family.

Finally, thank you to Shaun Barnabas. I would never have gotten this done without your comments, kindness and amazing patience. Thank you for everything you have done over the past few months, and for all the times you have coaxed me off the ledge with cute animal photos. Really, where would I be without you?

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
ASE	Adherence Self-Efficacy Scale
BMQ	Beliefs About Medications Questionnaire
CUMC-IRB	Columbia University Medical Center Institutional Review Board
HBM	Health Belief Model
HIV	Human Immunodeficiency Virus
HIV-KI	HIV Knowledge Inventory
HIV-TK	HIV Treatment Knowledge
KZN	KwaZulu-Natal
LMIC	Low- and Middle-Income County
LMUP	London Measure of Unplanned Pregnancy
MAA	Maternal Adherence Assessment
MCH-ART	Maternal and Child Health Antiretroviral Treatment Study
MOU	Midwife Obstetrics Unit
MTCT	Mother to Child Transmission
PMTCT	Prevention of Mother to Child Transmission
SES	Socio-economic Status
UCT-HREC	University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee
WHO	World Health Organization

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Part A:

Study Protocol

Adherence in HIV-Positive Women Entering Antenatal Care on Antiretroviral Therapy: A Cross-sectional Study

I. Summary

The Western Cape government has implemented Option B+ as the standard of care at all public sector clinics[1]. Option B+ dictates that once an HIV-positive woman presents for antenatal care at a government clinic, she initiates antiretroviral therapy (ART) for life. This is a major change from previous protocol, where women were only put on ART temporarily during pregnancy (Option A) or placed on lifelong treatment when their CD4 count dropped below 350 cells/µl. Option B+ eliminates the gaps between pregnancies and illness where a woman would not be on ART, leading to continuous care[1]. This will result in a growing population of women of child-bearing age who continue on ART and are expected to maintain adherence to their medication.

However, clinical studies of ART adherence have historically enrolled mostly male participants[2], and findings are often not reported by participants' sex[2,3]. It is known that barriers to adherence vary between the genders, and that women have been described as having lower levels of adherence than men[3,4]. Further, very little is known about the patterns of adherence among women conceiving on ART[5], who are a newly emerging population[6]. Pregnancy involves an additional set of complications for women that could further impede adherence [6]. These barriers might be different for long time users of ART, who are familiar and possibly more comfortable taking their medication than women who initiate ART for the first time during their pregnancy, however more study is needed into this new population.

We intend to address key questions surrounding this understudied population regarding the prevalence of poor adherence and significant factors associated with this outcome by conducting a secondary analysis of data collected during the Maternal and Child Health Antiretroviral Treatment (MCH-ART) study from a population of HIV-positive pregnant women who initiated ART prior to their current pregnancy and have presented at a midwife obstetric unit (MOU) in Gugulethu, Western Cape.

II. Introduction

2.1 Background

In 2013, the World Health Organisation (WHO) released guidelines that recommended all HIV-positive pregnant or breastfeeding women start antiretrovirals, and provided an option for these women to continue on lifelong treatment[7]. This recommendation was based on a modified programme adopted by the Ministry of Health in Malawi,[8] which came to be known as Option B+.

Early research on this new treatment protocol has shown positive outcomes. Modelled maternal outcomes were shown to be better, with increased maternal life expectancy[8]. It was posited that these women benefitted from uninterrupted treatment between pregnancies, simplified drug regimens, and not waiting for a low CD4 count to start treatment[8].

The Western Cape Department of Health adopted Option B+ as a treatment protocol for HIV-positive pregnant women in the public sector in July 2013[1]. When an HIV-positive woman presents at a public antenatal clinic, she has a viral load taken if it was not done in the past three months. If possible, she is switched to a fixed dose combination antiretroviral treatment; otherwise she is left on her current regimen. Adherence is checked throughout the pregnancy and continues to be monitored into the post-partum period, during which treatment continues [1]. Keeping these sexually active women of childbearing age on ART has led to an increasing population of HIV-positive women conceiving while established on treatment.

For South Africa, how well this growing group of long term ART users implement their medication if they become pregnant is of major concern. Adherence to ART is important during the antenatal period. Consistently taking antiretrovirals as prescribed has been shown to be the critical determinant in health outcomes for HIV-positive individuals[4]. Barron et al. found that about 70% of maternal deaths in South Africa in 2011 were associated with HIV infection[9]. Adherence to ART greater than 95% can lead to viral suppression, which helps maintain health and avoid progression to AIDS[4].

Not only does satisfactory adherence prevent maternal illness, but it will also prevent transmission of HIV to unborn children[5]. In 2007 about 300,000 babies were born exposed to HIV in South Africa[10]. Despite this high burden, mothers can protect their infants from exposure to the virus by simply taking their ART. Research from the European Collaborative Study found that every additional week of ART taken reduced the risk of vertical transmission of HIV to the foetus[11]. This protection extends into the postnatal period, as women who maintain a suppressed viral load are less likely to infect their baby with HIV via breastfeeding[12]. In short, satisfactory adherence to ART is crucial to maintaining the health of both mother and newborn.

There is also evidence to suggest that conceiving on ART provides improved outcomes for the infant. The European Collaborative Study found that the best paediatric outcomes were among women who conceived while established on ART[11,13,14]. They also showed that women who started ART before conception were more likely to achieve undetectable viral loads over the course of the study compared to those who started treatment after[13]. This low or undetectable maternal viral load is critical in the prevention of mother to child transmission (PMTCT) *in utero*[15]. These findings were supported by an additional study that found fewer cases of mother to child transmission (MTCT) in women who conceived on ART when compared to women who only initiated treatment during pregnancy[14].

Despite these positive outcomes, adherence to treatment is difficult as pregnant women have unique barriers to complete compliance. Women are already more likely to have worse adherence than men and more likely to be lost to follow-up in studies of adherence[3,4]. Pregnancy brings new obstacles[6], such as anxiety about the infant's HIV status; travel to the family home to stay after delivery; and inadequate partner support, especially among women who have not disclosed their status to their partners[10]. Additionally, fear of the potential harm ART could have on their unborn infant can cause women to become non-adherent during pregnancy[11]. These factors can make it near impossible for people who are otherwise willing and able to adhere to their medication to do so. A systematic review of antiretroviral adherence among pregnant women from all around the world found mean adherence of 50% to 61% for women during the prenatal period[5]. This further declined to 34 to 64% in the postpartum period.

Although there is poor reported adherence among this important group, there is a paucity of research into ART adherence among women, and even fewer articles written about adherence in pregnant women[5]. Clinical antiretroviral trials since 2000 have only recruited on average about 20% women for their study populations, making any insights that could be drawn from this small participant group too underpowered to be conclusive[2]. With respect to those who have initiated ART under Option B+, there is a call for more research into adherence and retention to treatment among this population[7]. The WHO's goal of elimination of MTCT by 2015[4] relies on ART adherence throughout the PMTCT cascade and bolstering support for women to ensure they are able to take their medication as prescribed.

2.2 Objectives

Primary Objective:

1. To describe the prevalence and determinants of adherence to antiretroviral treatment among HIV-positive pregnant women who initiated treatment before their current pregnancy and who presented for antenatal care at a Gugulethu MOU.

Key research question: How common is poor adherence to ART among HIV-positive pregnant women, and what are the significant causal factors for poor adherence among this population?

Secondary Objectives:

1. To describe the study population, looking at the distribution of socio-demographic variables and other risk factors measured.

Key research question: What are the prevalence and patterns of socio-demographic variables and measured risk factors in the study population? Do these patterns differ between participants that report satisfactory adherence and those who report unsatisfactory adherence?

2. To explore the agreement and validity of scale measures used to quantify study variables in this study.

Key research question: How valid are the tools used to measure these variables in the study?

3. To describe the relationships between the numerous self-reported measures of ART adherence taken in this study in order to select a valid outcome measure of adherence.

Key research question: How consistent and agreeable are the variables using different measures of self-reported adherence?

III. Methods

3.1 Study design

The MCH-ART study is unique in that it employs three phases on different sub-sections of the same participant population to answer different study objectives. Phases 2 is a prospective cohort that follows pregnant women eligible for ART initiation through three clinic visits into the postpartum period. Phase 3 is a randomized control trial with two arms comparing ART delivery methods for HIV-positive women who have recently delivered. Phase 1, the phase from which these study data and analysis will be derived, used a cross-sectional survey at an MOU in Gugulethu, Western Cape. Participants were sampled consecutively for this phase of the study, and enrolment lasted from April 2013 through May 2014.

3.2 Population and sampling

Population

For this analysis, women were considered for inclusion if they were over 18 years of age, pregnant and HIV-infected. Women needed to have started ART prior to their current pregnancy, which was defined as being on ART for at least four months prior to enrolment. HIV status was confirmed by either two positive rapid tests or supporting documentation brought in by participants. Either an ultrasound, urine test or clinical assessment was used to confirm current pregnancy.

Participants were excluded if they were not currently pregnant or if they had a medical, physical or social condition that would preclude them from properly consenting or participating in the study. These conditions included, but were not limited to, denial of HIV status and refusal to take ART.

Method of sampling

Consecutive patients were sampled for this phase of the study. At their first visit to the MOU, women were briefly informed by unit staff of the MCH-ART study and those who expressed interest in participating were introduced to study staff. Prospective participants were then given more information about MCH-ART by study workers. Informed consent (see protocol Appendix A) was attained by study workers from women who met inclusion criteria and who expressed a desire to participate in Phase 1 of the study only.

Sample size

Using this procedure, 1,544 women were recruited for this phase of the MCH-ART study. Of these women, 535 were reported having been on treatment for at least four months. This was considered long enough to have been able to conceive on ART. Further analysis of treatment history taken from data abstraction of medical records, 33 participants were dropped from the data set as their start date for treatment was less than four months before their MOU visit date, meaning that they were not considered to have been established on ART prior to their current pregnancy. A total of 486 participants met all the criteria for inclusion and had no missing data.

3.3 Measurements

After consent was given, participants completed a 20-minute series of questionnaires that gathered information on demographics and various risk factors for ART non-adherence (see protocol Appendices B-I). The questionnaires were administered in either English or isiXhosa to participants by study staff.

Instruments

The following tools were used in Phase 1 of the MCH-ART study (see protocol Appendices B-I):

1. Demographics and Medical History
2. HIV Treatment Knowledge Inventory[16] (adapted)
3. HIV/AIDs Knowledge Inventory[17] (adapted)
4. Adherence Self-Efficacy Scale[18]
5. Beliefs about Medications Questionnaire[19]
6. London Measure of Unplanned Pregnancy[20]
7. Family Planning Use/Intentions
8. Maternal Adherence Questionnaire[21]

Among the questionnaires put to study participants were those designed by investigators for use in the MCH-ART study. These included questionnaires on demographics, socio-economic status and medical history; and family planning and intention to become pregnant. The other measures used in the study were sourced from published peer-reviewed articles. These measured participants' knowledge of HIV and HIV treatment; ART medication beliefs; pregnancy intentions; self-efficacy and confidence in taking medication; and ART adherence.

After completion of the questionnaires, 5 ml of blood was collected to assess participants' viral loads. Specimens were batch tested using an Abbott Molecular RealTime HIV-1 assay (Abbott Molecular, Illinois, USA).

Outcome of Interest and Independent Variable

There is no agreed upon method of measuring adherence to ART used in pharmaceutical or epidemiological studies[22]. Neither is there an agreed upon percentage of medication a participant must take as advised to denote “good adherence”[23]. The best adherence can be defined as is “the level to which patients follow medical advice or treatment plans such as taking medications, keeping medical appointments and maintaining lifestyle changes”[5].

Phase 1 of the MCH-ART study uses a few different self-reported measures of participants' adherence to their medication (see Protocol Appendix I):

1. Self-reported number of missed doses of antiretroviral medication in the past 30 days
2. Self-reported Likert scale of adherence to antiretroviral medication in the past 30 days
3. Self-reported Likert scale of adherence to antiretroviral medication since initiation of treatment

After careful consideration, it was determined that a binary variable separating participants into those who missed no doses of ART in the past 30 days and those who missed one or more doses should be the outcome of interest.

Table 1: List and definition of variables that will be examined for analysis of Phase 1 data:

Variable	Definition	Scale
Demographics		
Age (years)	Participant age	Numerical (continuous)
SES Category	Composite score derived from participant employment status; level of education attained; number of assets; housing type; and whether or not participant receives any social grants. This raw score was then categorised into low, middle and high.	Categorical (ordinal)
Education	Level of school participant had completed	Numerical (discrete)
Employment	Whether participant was employed	Categorical (binary)
ART Duration	Number of months participant has been on treatment	Numerical (continuous)
CD4 Count	Taken from participants' raw CD4 counts and made into three categories: <350; 350-499; and 500 and over	Categorical (ordinal)
Viral Load	Taken from participants' raw viral load and made into two categories: Detectable (>50) and undetectable (≤50)	Categorical (binary)
Intrapersonal		
Self-efficacy	Composite score taken from participants' responses measuring their self-efficacy and confidence in taking their medication and following guidelines. Taken from a 15-item scale, with responses ranging from “Not at all confident” (1) to “Very confident” (5). The higher the score, the more desirable responses given.	Numerical (discrete)
Medication beliefs	Composite score taken from participants' responses measuring their confidence and perceptions towards their medication. Taken from 7-item scale, with participants agreeing, disagreeing or saying they did not know. The higher the composite score, the more responses the participant gave that demonstrated a positive belief in their ART.	Numerical (discrete)
Maternal Adherence	Composite score taken from participant's responses ranking their adherence to their medication. Drawn from four scale items, the higher the composite score, the better the self-reported adherence.	Numerical (discrete)
London Measure of Unplanned Pregnancy	Taken from the questionnaire with the same name, this measures the intentionality of the participants' current pregnancies. The higher the raw composite score the more intentional the pregnancy	Numerical (discrete)
HIV Treatment Knowledge	Composite score taken from participant's responding either “True,” “False,” or “I don't know” to statements concerning antiretrovirals. A point was given for a correct response, and no points for an incorrect or “I don't know.” The higher the composite score, the more correct responses given	Numerical (discrete)
HIV/Aids Knowledge Inventory	Composite score taken from participant's responding either “True,” “False,” or “I don't know” to statements concerning the transmission or science of HIV/Aids. A point was given for a correct response, and no points for an incorrect or “I don't know.” The higher the composite score, the more correct responses given	Numerical (discrete)
Interpersonal		
Disclosure status	Whether or not a participant has disclosed their status to another person	Categorical (binary)
Male partner disclosure	Whether or not a participant has disclosed their status to their current male partner	Categorical (binary)

3.4 Limitations

Selection Bias

This cross-sectional survey was conducted on a group of HIV-positive women established on ART and attending a MOU at their fourth month of pregnancy. This sampling frame excludes those HIV-positive women who do not seek antenatal care or who book for care later in the pregnancy. This group of women might have a different level of adherence and separate risk factors for poor adherence than the women who received timely antenatal care and were sampled. The differences between these groups cannot be assessed, as data on HIV-positive women not at the antenatal clinic could not be collected by virtue of them not being present to be sampled in this cross-sectional study. Keeping this in consideration, the study population must be carefully defined in the analysis and subsequent reporting of the study's findings.

Information Bias

Not all participants sampled for this analysis have complete data. Where a participant is missing data for a questionnaire, they will be dropped from the analysis. However, these participants will be compared against the rest of the study population to ensure that they are not different with regard to the frequency of the outcome or other major risk factors.

The outcome measure used in this analysis will be a self-report of adherence. As with all self-reported measures, there is a potential for bias here. Self-reported measures of adherence are notoriously less reliable than other objective measures, such as refills or claims-based measures[24]. However general correlation between self-reported adherence and MEMs cap, an objective measure, has been shown[25]. To show some internal validity, the selected outcome measure will be compared against other self-reported adherence measures used in the survey to assess their correlation.

Confounding

One of the limitations of this analysis is that during Phase 1, data were not collected on some potential risk factors identified in a review of the literature. We will not be able to adjust for the effect of barriers to adherence previously identified through a review of the literature, such as alcohol consumption[26], depression[16,26], and experiencing medication side-effects[24]. As such, there is potential for confounding that cannot be adjusted for.

IV. Analysis plan

All quantitative analysis will be conducted using Stata Version 11.0 (Stata Corporation, College Station, Texas).

Secondary Objective 1:

Proportions of participants' demographics and reported risk factors will be calculated. The distribution of these variables in the population will be examined with special attention given to those factors identified in the literature as potential risk factors. This background information on demographics and self-reported adherence measures will be tabulated to describe the population.

Risk factors identified during a review of the literature will be compared between participants who missed no doses and those who missed one or more doses in the last 30 days, to contrast between outcome groups. Chi-squared tests or Fisher's Exact will be used for categorical variables and two-sample t-tests or rank-sum tests for numerical variables. All tests will be analysed using a cut-off of 95% for the significance level.

Secondary Objective 2:

Six separate tools were used to measure risk factors in this population. The “HIV Treatment Knowledge” and “HIV/AIDS Knowledge Inventory” tools used true and false questions to assess study participant's knowledge of their disease and treatment, also giving an option for “I don't know.” Composite scores will be generated for all participants for each of these measures, giving a point for a correct response and no points for an incorrect response or “I don't know.”

The other four tools used Likert scales to assess how participants rated their self-efficacy; their belief in their medications; their adherence to their medication; and the intentionality of their pregnancy. Composite scores will be generated for these tools as well, with higher points given for more favourable responses (i.e. a response that indicated greater confidence in medication keeping a person healthy would receive a six).

For all of these scales, a Cronbach's alpha will be calculated to assess the performance of these tools on this population. Any alpha above 0.7 will be considered acceptable, and will be considered in looking at the validity of the composite scores for participants and their inclusion in the model building process.

Secondary Objective 3:

Participants will be split into two groups based on whether they self-reported missing no doses in the past 30 days, or missing one or more doses. Other self-reported adherence measures, such as self-rating of adherence since initiation and in the last 30 days, will also be compared between these two groups to assess correlation and consistency between the measures of adherence. To further explore and validate the chosen outcome measure, participant's viral loads will be compared to their self-reported missed dosage. This will be done using chi-squared tests, comparing the missed dose categories to detectable and undetectable viral load. All tests will be analysed at 95% level of significance.

Primary Objective:

Finally, a logistic regression model will be constructed using significant variables identified in the bivariate analysis. The variables will be fit in three stages, separating the risk factors into socio-demographic, intrapersonal and interpersonal risk factors, a method of organising these variables that evolved from ideas in Clouse et al.[6].

A table will be constructed that displays these stages of model building that reports odd ratios and 95% confidence intervals to show significance. Panel 1 will show empty models for each of the significant variables, exploring their unadjusted relationship to the outcome. Panel 2 will adjust for hypothesised associated demographic variables and individual risk factors separately to give adjusted odds ratios. Panel 3 will start to build the final model, adjusting for associated demographic variables and significant intrapersonal variables together. The final step will be in Panel 4, which will fit both significant intrapersonal and interpersonal factors into a logistic regression model.

V. Ethics

Ethical approval for the MCH-ART study was attained from University of Cape Town's Faculty of Health Scienes Human Research Ethics Committee (UCT-HREC) and the Columbia University Medical Center Institutional Review Board (CUMC-IRB) (see protocol Appendix J). The two boards reviewed the study protocol, informed consents, questionnaires, procedures and other associated documents before giving their final approval. Both organisations also follow up with the MCH-ART study on an annual basis to review its progress.

This analysis of already-collected data from the MCH-ART study does not present any potential risks to the women who participated in this study. All of the data that will be analysed have been anonymised, and

the only identifying marker for study participants is the patient ID they were assigned at enrolment. The graduate student undertaking the analysis will not have direct access to participant files or medical records that have been abstracted. In the event that the graduate student needs access to the original forms to check a discrepant response, the graduate student will be supervised by the MCH-ART study manager and/or the student's advisor.

VI. Stakeholders, reporting and implementation

Upon completion of analysis and revision, an article from the findings of this secondary analysis will be published in a peer-reviewed journal. Through publishing, the findings of this study will be made public and will help to inform academics and medical practitioners working with similar patient populations. We believe that medical practitioners, public health researchers and policymakers involved in the areas of PMTCT and maternal health will be interested in the findings from this analysis. It is hoped that by sharing the findings of the analysis of Phase 1 data from the MCH-ART study, greater light can be shed onto the barriers of adherence among HIV-positive pregnant women currently on ART, an understudied and yet incredibly important group.

VII. Logistics

As this is a secondary analysis of data that has already been collected from a study that has already received approval from CUMC-IRB and UCT-HREC, very little remains in the way of logistics. All that remains for the graduate to do is to finalise and write a review of the literature, to conduct the outlined analysis of the data and to write-up the final article for submission in her thesis.

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Part B:

Literature Review

I. Introduction

Adherence to medication is a complicated and nuanced issue. What constitutes adequate adherence to any one treatment differs with the medication studied, depending on the pharmacology; the population being studied; the number of pills skipped or taken incorrectly over a specific time period; how long that time period is and how representative that time period is of that person's life[1,2].

These complications ring especially true with regards to the study of antiretroviral therapy (ART) for the management of HIV[3]. There is no agreed upon method for measuring ART adherence, or even what percentage of pills a participant must take correctly to be considered adherent[4]. Generally, the percentage of ART taken that is considered good adherence ranges from 80% to the strict 100%[5], however the study reporting that range found no significant difference in survival for patients who reported between 80-99% and total adherence. For ART patients, adherence of 95% or better is required to achieve viral suppression[1]. This means not missing more than one pill a month[6].

Despite these differences, adherence to ART remains the determining factor in HIV treatment outcomes[6]. ART is crucial in delaying illness and maintaining health, as poor adherence significantly increases the risk of death in HIV-positive individuals. This is due to the close relationship between ART implementation and a high viral load being associated with disease progression and adverse health outcomes[1,7]. A suppressed viral load leads to better long term health outcomes and longer life in this population[1,4,5].

Additionally, good adherence can make transmission to another person more difficult through a suppressed viral load[1,6]. This benefit is critical for neonate health[7]. A low viral load helps in the prevention of mother to child transmission (PMTCT), allowing children born to HIV-positive mothers to avoid infection *in utero* and in the postnatal period[8–10]. This is of major importance to South Africa, where nearly one out of every three pregnant women is HIV-positive[11]. It is a necessity to public health in South Africa to better study adherence and characterise the barriers pregnant women face in taking their medication.

There is a gap in the knowledge when it comes to women's adherence to ART, especially among the growing population of HIV-positive pregnant women who have been established on ART before presenting for antenatal care[1]. Though this is an established population of HIV-positive women in more developed areas, like Western Europe[12], the implementation of treatment protocols like Option B+ in less developed countries[13] will result in new subsets of this group now beginning to emerge. A 2014 study of HIV-positive

postpartum women in Johannesburg found that 30% of those interviewed had initiated ART prior to pregnancy, with a median duration of 2.6 years[14].

The complexity of adherence and the lack of agreement within the scientific community as to what constitutes being "adherent"[1,5] leave room for research into ART adherence and exploration of differing definitions of that outcome. The aim of this literature review is to identify current issues in adherence research in pregnant women, with special attention to studies that speak to the barriers faced by women who are long time users of ART. It will serve to highlight current issues in adherence research, such as the reliability of measures of adherence, differing definitions of good adherence and risk factors for poor adherence. This is to better inform the primary purpose of this thesis: To describe the prevalence and determinants of adherence to ART among HIV-positive pregnant women who initiated their treatment before their current pregnancy and who presented for antenatal care at a Gugulethu midwife obstetrics unit (MOU).

1.1 Literature Search Strategy

A review of the literature was conducted through Google Scholar and Pubmed for scholarly reviewed papers published up until December 2014. Search terms included the following terms in combination and alone: "adherence", "pregnancy", "ART", "HAART", "nevirapine", "antiretroviral", "conceive", "initiate", "South Africa", "Cape Town", "viral load", "Option B+", "HIV", "PMTCT", "European Collaborative Study". Conference proceedings, book chapters and government policy handbooks were also included in this review, along with systematic reviews and meta-analyses.

II. Background

In 2013, the World Health Organization (WHO) released updated guidelines that recommended all HIV-positive and breastfeeding women initiate antiretrovirals and gave an additional option for women to continue lifelong treatment after giving birth[15]. This plan, which came to be known as Option B+, was quickly adopted by the Malawian government[16]. Modelling of maternal health outcomes were shown to be better under Option B+, with increased maternal life expectancy[17]. This same study also showed that women benefit from Option B+ by starting treatment earlier, having no treatment interruption between pregnancies and not waiting for a low CD4 count to start treatment for life[17]. They posited that simplifying treatment regimens and delivery would decrease transmission and improve retention outcomes among women.

Eliminating interruptions in ART for women who have already had a child will also benefit those who might go on to have an unplanned pregnancy. Studies have found a significant portion of pregnancies among HIV-positive women are in fact unintended[12], with it estimated that just over half of pregnancies in HIV-positive European women are unplanned. This is important in South Africa, where unplanned pregnancy is common in some areas. In a cross-sectional survey of pregnant women in KwaZulu-Natal (KZN), 86% of participants said their pregnancies were unintended[18]. Extending ART coverage past the postpartum period means also extending coverage to the early days of these potential unplanned pregnancies, when the mother might not otherwise know she is pregnant and before she presents for antenatal care.

However, the WHO has called for more research into adherence and retention in antiretrovirals on this new plan, over concerns with long-term retention on ART because of initiation happening much sooner for women and the acceptability of this change[15]. There also remain questions over the change in messaging, as women who were previously told to only come in for ART when feeling sick are now expected to initiate and maintain treatment for life regardless of whether they feel healthy[15].

III. Concepts and Definitions

3.1 Outcome

Measuring Adherence

There is no gold standard measurement of adherence widely embraced by researchers[3,4], and all measures come with their own drawbacks. With measurements of adherence, researchers must weigh reliability, richness of sampling and feasibility[2]. Different study purposes require assessment tools with different sensitivity[3] to adequately quantify adherence. For self-reported measures, phrasing is also an issue. Changes in how a question is presented, such as ranking adherence on a scale of 1 to 10 compared to assigning an adjective to describe their adherence can greatly affect responses[19].

In his presentation at the 2014 HIV Research for Prevention conference, Terrence Blaschke singled out recall questionnaires of adherence as being unreliable and providing sparse information for clinical trials of medication[2]. Generally, self-report and patient diaries, though cost-effective and quick, are notorious for recall bias and having low reliability[6]. Electronic monitoring systems and biological measures can provide more reliable measures, but are often unrealistic for most studies[2]. Self-reporting can exaggerate the incidence of good adherence, showing higher levels of adherence to ART amongst HIV-positive participants when compared to pharmacy refills or “claims-based measures”[7]. In contrast, Oyugi et al. found good agreement between patient self-report, pill counts and MEMSCaps[20].

Adherence in South Africa

Low- and middle-income countries (LMICs), and even resource poor settings in more developed countries, can provide unique barriers to adherence. In South Africa specifically, antiretroviral stock outs, long lines at clinics and issues with transport can frustrate patients and prevent them from accessing their medication[14]. Qualitative interviews of South African HIV-positive participants brought to the fore people's fear of status disclosure by clinic workers, or being deduced by community members. Clouse et al. found that women who continued to seek medical care after giving birth to their infants were viewed with suspicion by their community[14]. This perceived stigma caused some women to skip clinic visits and become non-adherent to their medication[14].

But studies of adherence to ART in LMICs have shown promising results. HIV-positive people from Africa had a higher percentage of adherent patients compared to those in North America according to a meta-analysis from Mills et al.[5]. In another meta-analysis, 77% of African patients took over 80% of their medication correctly, meeting the study's definition of good adherence[6]. Nachega et al. did bring up issues of over reporting of adherence in studies conducted in Africa, as these studies tend to have shorter follow-up time and more self-reported outcomes than compared to studies in more developed regions[4].

Poor access to resources does not necessarily mean health services are unavailable. Boyles et al. showed that successful service delivery is possible in resource-constrained settings[21], meaning that antiretrovirals should be available in overstretched community clinics. Supporting this, in a 2004 Soweto study of antiretroviral adherence in a resource-constrained setting, 88% of participants reported greater than 95% adherence for the previous month[22]. A systematic review and meta-analysis[7] had South African studies reporting 60% to 86% of their participants reporting adequate adherence, though studies differed in definition of adherence and methods.

Adherence in Women

The story of ART adherence in women is a complicated one. From the start, women are underrepresented in clinical trials of ART among HIV-positive people, as drug trials of antiretrovirals since 2000 have recruited about 20% women on average[23]. There are some studies, like Nachega et al., which found that women were more likely than men to have adherence higher than or equal to 80% amongst South Africans[4]. However, women generally have poorer adherence than do their male counterparts[7]. Heterosexual women had the lowest rates of adherence in a study of recalled medication adherence from the previous three days among gay men, heterosexual men and heterosexual women in the United States[24]. Only one woman reported perfect adherence compared to 15 gay men who reported perfect adherence.

Women fare worse with regards to adherence for a variety of reasons. A number of studies suggest that, because women are more likely to place greater importance on their relationship with others and their standing within their community, their adherence suffers because of issues around disclosure and self-efficacy[23,25]. Anderson et al. found that women's experiences with depression, stress, stigmatization and the importance placed on social relationships affect adherence, making it generally less than that of men[23]. A study of pregnant women in Western Europe found that participants with at least two children already had poorer adherence to ART than those with no previous children[26]. This could indicate challenges women face caring for their families while maintaining adherence to medication[26].

Adherence during Pregnancy

The literature shows that pregnant women have an even harder time remaining on treatment. A systematic review of antiretroviral adherence among pregnant women from all around the world found average adherence of 50% to 61% for women during the prenatal period[1]. This study went on to find that adherence declined to 34% to 64% in the postpartum period. A South African study showed that about half of women dropped out of HIV care after delivery[14]. Wang et al. found that women were more likely than men to be lost to follow-up six months after initiating ART[11]. In this study, pregnancy status, along with gender, were the only factors significantly associated with being lost to follow-up at six months. A cohort study in the Eastern Cape found that women who initiated ART for the first time during pregnancy were over three times more likely to be lost to follow-up at the end of the study period than those who did not initiate ART in pregnancy[21].

There are unique problems for HIV-positive women who conceive their infants after having already initiated ART, as they not only have to navigate issues related to their pregnancy, but may also have to deal with changes in ART regimen and side-effects from their medication[1]. But very little study has been done on this group. Some studies have been conducted on long term ART users in Europe[8], however there is a paucity of information on adherence in pregnant women in developing countries[1]. The barriers to adherence in this population have not yet been described in a study, leaving an important niche for future research.

3.2 Risk Factors

The list of barriers to adherence for pregnant women is long, and includes factors such as lack of partner support; anxiety about their infant's HIV status; and little motivation to adhere to lifelong medication after a healthy delivery[14,27]. However, this literature review will only focus on those issues addressed in Phase I of the MCH-ART study, leading to the omission of some important risk factors identified in other studies of antenatal ART adherence. For this review, risk factors were organised into three separate categories: socio-demographic, interpersonal and intrapersonal[14].

Socio-demographic factors

Age

A number of demographic factors come into play when looking at adherence among HIV-positive women. Young age was found to be a barrier to adherence in a systematic review of pregnancy ART adherence studies, and being an older mother was shown to be more likely to contribute to good adherence[1]. A literature review found reduced adherence was associated with young age in women[25]. Young age has also been linked to post-partum loss to follow-up[10].

Socio-economic Status

Financial issues have also been shown to be a barrier to adherence[1]. Qualitative studies profiled by Vitalis have highlighted the high cost of transportation, widespread poverty and financial dependence on a partner as barriers to adherance[1]. These are costs that someone of low socio-economic status (SES) would not be able to cope with[14,28]. Interviews with women in KZN identified lack of food and finances as a barrier to adherence[29]. Some women reported not disclosing their status to their partner, and thus hiding their ART, because they fear rejection[30]. For a woman in a relationship with a man where he is the financial provider, aside from the emotional trauma of possible rejection, a partner leaving them because of their HIV-status means the loss of financial stability[30]. Such dependency might make women less able to negotiate with their partner, impeding the use of ART or exclusive formula feeding of a newborn for PMTCT[28].

Though some studies have shown a positive link between SES and adherence, their relationship is not clear in the literature. Chesney et al. found that those who worked outside the home for money were actually more likely to report episodes of non-adherence in the previous two weeks[31]. Other studies have not found significant differences between good and poor adherers with regard to SES[22].

Level of schooling

Education is also a major demographic factor in studies of adherence. For example, more years of formal education were significantly associated with better medication adherence from the past three days[24]. A lower formal education has been identified as a barrier to adherence[25]. Similarly, mothers with no high school education were shown to be less adherent in the administration of Nevirapine to their babies postnatally compared to mothers with a high school education[32] .

Intrapersonal factors

Medication Beliefs

A woman's belief in her medication is a factor in how well she adheres to it[1]. Horne et al. found in their paper, where they introduced a new method of assessing medication belief, that the beliefs a person holds about their medication are likely to inform how they take it[33]. This determines if and when a patient takes their medication, if they take it as recommended by a health professional and whether it is continued[33]. Malcolm et al. found that the HIV positive patients with excellent adherence in Rhode Island who they sampled believed that 90-100% adherence was necessary to benefit from their medication[34]. HIV-positive participants with “greater perceived treatment efficacy,” “stronger belief that combination therapy is a significant treatment advancement,” and “greater hope that combination therapy would be effective” had better adherence[24].

HIV and ART Knowledge

Similarly, a person's knowledge of their medication can be a very important influencing factor in their adherence to it. Wagner et al. found that greater knowledge of HIV treatment and understanding of the effects of poor adherence was associated with better ART adherence in a survey of serodiscordant couples[24]. A survey of ART patients in Rhode Island found that those who did not understand how their medication affected the virus had poorer adherence[34]. Misinformation about HIV prevention can be a huge barrier to accessing health services[35], and can play into perceived stigma of HIV-positive people. Women need to understand the necessity for continued ART use because HIV-positive antenatal care attendees who do not otherwise feel ill are most at risk to be lost to care after delivery because they feel they have no incentive to continue lifelong treatment[10].

Pregnancy Intention and Foetal Wellbeing

Pregnancy intention is a complicated issue that involves the context under which the woman fell pregnant; the woman's stance on being pregnant; and the behaviour she undertook to either plan for or prevent the pregnancy[36]. Quantifying these ideas into a single pregnancy intention for participants helps researchers to conceptualise participants' attitudes towards their pregnancy without reducing these intentions to a couple of categories. Pregnancy intention could further characterise a woman's preparation for her unborn child, such as taking antenatal supplements[36], and might speak to her concern for her unborn child's health and dedication to taking ART for PMTCT.

A 2008 study found that women adhered better during their pregnancy than at a 6-month check-up[27]. Of these women who reported better adherence during pregnancy, 90% said they did so because of concern for their baby's health. Of these women who cited foetal well being as their primary reason for adherence, only 18% reported complete adherence postnatally[27]. Qualitative interviews at Cape Town public-sector primary care clinics and referral hospitals offering services to pregnant women, including ART services, showed that women adhered to ART in pregnancy to protect their children[10]. Concern for their child was found to be a major facilitator of adherence among HIV-infected pregnant women[1].

Inversely, concern for the foetus and its safety can also be major barriers to ART adherence as women's poor adherence comes from their need to protect their children from the perceived harm of medication[1]. Women put their children's health before their own after birth, sometimes sacrificing good adherence to care for their newborns[10]. In a survey by Clouse et al., 29.2% of women cited putting the baby's health before that of the mother as a reason why women were not adherent to ART[14].

Self-efficacy

Self-efficacy is a person's belief in their own competence to achieve long term goals[37]. Self-efficacy has been shown to be an important factor for health behaviours for some chronic conditions[38]. It is especially important for those with HIV, as a new diagnosis can lead to feelings of “social isolation, despair and powerlessness”[39]. If these feelings persist, they can make treating a person’s HIV difficult. Because of this, a lack of self-efficacy has been identified as a barrier to adequate ART adherence in the literature[1,40].

Chesney et al. looked at correlates of non-adherence to ART in the previous two weeks in both men and women in the US[31]. They found that those who were less certain that they were capable of taking all or most of their medication as directed were more likely to report non-adherence[31]. Doherty et al. found low levels of reported self-efficacy in their cohort of HIV-positive South African mothers, and many participants also doubted their ability to care for their children[39].

Interpersonal Factors

Social support

Support from family, friends and partners has been found to have a positive influence on adherence among pregnant women[1]. However, fear of losing this support by disclosing to friends and family can be equally as damaging to adherence. Interviews with women seeking antenatal care at public sector facilities around Cape Town showed fear of disclosure because of the threat of abandonment by their partner, and that this idea was common among women in relationships[10]. Promisingly, the study found that when the majority of these women did disclose to their partner, they had positive, supportive experiences. In a US study, patients who were open with family and friends about their HIV status were more likely to be excellent adherers to their medication than those who had not disclosed[34].

Women who have not disclosed often must make concerted efforts to make sure their family and neighbours do not discover their status. This can negatively impact adherence if they have to hide their medication or take it at times when people are not around[41]. Dahab et al. found that both patients and health-care workers cited fear of stigma as a barrier to adherence and to modifying treatment adherence to suit their current circumstances[40]. This is dangerous, as having to hide medication can lead to taking it earlier or later than indicated and not achieving therapeutic levels for long enough to suppress viral load[6].

Partner involvement

Partner involvement can be a determining factor in adherence for serodiscordant couples. A Stinson and Myer article showcased quotes from a series of interviews done with healthcare workers, in which one lamented that women bring in treatment partners for support in taking and/or beginning ART, but then "…'Usually the treatment buddy is a partner and then we lose them…. They don't come back…. They don't start because of a treatment buddy problem'"[10]. Another study found that lack of male involvement, lack of trust and confidentiality with healthcare workers and being a single woman were associated with mothers not taking nevirapine[32]. In this study, participants' telling their partner about nevirapine was associated with maternal adherence, and father of the baby attending antenatal care visits was associated with HIV disclosure to male partner[32].

Stigmatization

Building off this, fear of stigmatization is another societal barrier to disclosure, and as such is also a barrier to adherence. Turan and Nyblade described anticipated stigma, enacted stigma, perceptions of stigma and internalized stigma as all being potential negative psychosocial effects a women might

experience if she discloses[41]. In a later study, they found that stigma was a barrier to service uptake and adherence throughout the PMTCT cascade[41]. Women who experienced internalized stigmatization and thought that HIV-positive people should be ashamed, were far less likely to report having used antiretrovirals than women who did not carry this same stigmatization[41]. A study of healthcare workers revealed that they believed women who had difficulty accepting their HIV-positive status and displayed signs of internalized stigma, appeared less likely to initiate ART during pregnancy[10]. HIV-positive pregnant women have a harder time during pregnancy, as they might deal with an additional layer of stigma and judgment for getting pregnant and putting their unborn child at risk of HIV infection[41]. This is a complicated issue and plays into issues surrounding foetal well-being, and perceptions of poor motherhood.

IV. Benefits of ART Adherence

The benefits from having women, especially pregnant women, adhere to their treatment certainly outweigh the issues of getting them to take their medication properly. In South Africa in 2011, about 70% of maternal deaths were associated with HIV-infection[42]. Full adherence to treatment helps to keep women healthy by suppressing their viral load and decreasing their risk of developing illnesses associated with being HIV-positive[7]. Further benefit can be derived from the fact that taking ART during pregnancy greatly reduces the risk of a mother transmitting HIV to her child *in utero*. The European Collaborative Study found that every week of antenatal ART taken decreases the risk of vertical transmission of HIV to the foetus[10]. However, the success and gains expected from expanding ART to lifelong coverage for all HIV-infected pregnant women depends on the proportion of those women who adhere properly to treatment and remain in care[14]. Because in South Africa 50% of women drop out of care after delivery[14], finding a way to support ART use in the post-partum period is crucial. Continued treatment into the post natal period leads to a continually suppressed viral load for the mother and therefore better health outcomes, and ART helps to prevent transmission of HIV to the infant through breastfeeding[12].

Conceiving while on ART leads to good health outcomes for the child. There are fewer instances of MTCT for women who conceived on ART when compared to women who initiated ART during pregnancy[9]. In fact, women who started ART before becoming pregnant were more likely to achieve undetectable viral loads over the course of a European Collaborative Study compared to pregnant women who started ART antenatally. That study also found that the infants with the best outcomes were born to mothers who started ART before their pregnancy[8]. Further driving the point home, Hoffman et al. observed no *in utero* transmissions among women who were on ART for more than 32 weeks before delivery[9].

Improved adherence to ART could have huge impacts for HIV-positive women in South Africa. There is a high burden of HIV in this country, especially among pregnant women. About 1 out of every 3 pregnant women in South Africa are HIV-infected[11]. It was estimated that in 2007, 300,000 babies were born exposed to HIV in South Africa[32]. This is a huge number of children who have the potential to be born HIV-positive, and are therefore at risk for poorer health and early death than their HIV-negative counterparts.

The benefits from widespread ART use could extend to the population level. If good adherence to ART was widely adopted amongst HIV-positive individuals, there would be a higher prevalence of suppressed viral loads and possibly fewer transmissions to negative individuals[24]. Though still in need of study, widespread good adherence could further lead to a lesser burden on the health care system and lower costs associated with HIV care. This is because better adherence could lead to fewer hospitalizations for conditions associated with untreated HIV[6]. There is also a danger from widespread non-adherence as well. Poor and intermittent adherence to ART can lead to drug-resistant strains of HIV, which might then be transmitted on to other people and lead to available and cheaper first-line HIV medications becoming ineffective[1,6].

V. Conclusion

There is no doubt that taking ART consistently and as prescribed can lead to viral suppression[1], and that the longer a person is on treatment the better off they are[9]. Viral suppression can, in turn, lead to better health for an HIV-positive individual[1,6,7]. It can also impede the transmission of HIV to others[24], including *in utero* transmission[10], making it a critical component of an HIV-positive woman's antenatal care[14]. If treatment is continued, this protection extends into the postnatal period[12].

It is accepted that long time users of ART are an emerging population in South Africa[14]. With the adoption of Option B+, women of child-bearing age will be put on ART at their first pregnancy, continuing to take their medication for the rest of their life[13]. This is good news as pregnant women who are established ART patients have been shown to have better health outcomes for their infants[8].

It is also known that there has been little dedicated study done on this growing population of women[1]. Without any insight into the barriers to adherence specific to this group, clinicians and researchers simply have to extrapolate from other groups with overlapping characteristics (i.e. long term users of ART; HIV-positive women initiating ART for the first time at pregnancy). This, however, does not accurately describe these women's experiences and does not help health care providers to support adherence in this group.

My dissertation addresses this gap in the knowledge by focusing exclusively on HIV-positive women in a LMIC setting who conceived while already on ART. This analysis looks at a wide variety of factors associated with adherence in previous studies conducted in other populations to explore their associations to good adherence in this population. This research is a first step into characterising the experiences of this population in maintaining good adherence to ART, and will hopefully spur further interest in this area of study.

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Part C:

Journal Article

Formatted for submission to the Journal of Acquired Immune Deficiency Syndromes (JAIDS) (Epidemiology and Prevention Section)

Adherence in HIV-Positive Women Entering Antenatal Care on Antiretroviral Therapy: A Cross-sectional Study

Running head: Self-reported antenatal adherence to ART

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Conflicts of Interest: The authors have no conflicts of interest to declare

Funding: The MCH-ART study is funded by a grant from the National Institutes of Health

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UCT MPH guidelines direct that advisors not be listed as authors on a dissertation's Part C: the journal ready manuscript, and instead have their contribution to the finished work mentioned in the Acknowledgements. Though this article was written according to the guidelines for JAIDS, it directs that all authors be listed on the covering page, along with their affiliations and degrees. As per UCT MPH guidelines, Prof. Myer's contributions will be recognized in the acknowledgements. Detailed formatting instructions for JAIDS can be found in Part D, Appendix IV.

Abstract

Word Count: 3500
Abstract: 247
Tables: 5
Figures: 0
References: 33
Keywords: Adherence, ART, pregnancy, South Africa, Option B+, PMTCT

Background: With the adoption of Option B+ in the Western Cape, there is a growing population of women who are long-term users of antiretroviral therapy (ART). For some of these women, this results in conceiving on treatment as they no longer stop ART between pregnancies. However, limited research has been done into the barriers of adherence among this emerging group.

Methods: From April 2013 through May 2014, cross-sectional data was collected from participants of the MCH-ART study who initiated ART prior to their pregnancy. A statistical analysis was then conducted, looking at correlates of good adherence.

Results: Of the 486 women found to be established on ART prior to pregnancy, 78% reported not missing a dose of the ART in the past 30 days. In a logistic regression, a unit increase in the scores of medication belief, self-efficacy and pregnancy intention all had a positive association with participants reporting perfect adherence. Those of low socio-economic status were found to be more likely to report not missing a dose when compared to middle and high socio-economic levels.

Discussion: Generally high levels of adherence were reported in this group, as 85% of women missed one or fewer doses of ART in the last 30 days, giving them good enough adherence to potentially achieve viral suppression. The results of this analysis are an important first step into characterising the barriers of adherence in this growing population. Further research could assist health care workers in identifying barriers to adherence in pregnancy.

This article meets the requirements for Epidemiology and Prevention manuscripts as set out in the Online Submission and Review System Guidelines for the Journal of Acquired Immune Deficiency Syndromes. In keeping with these guidelines, tables referenced in the text can be found after the references.

Introduction:

Viral load is a crucial factor in an HIV-positive person's health. A suppressed viral load, where HIV reaches low or undetectable levels in a person's blood, has been shown to lead to improved health outcomes and longer life. But achieving suppression requires good adherence to antiretroviral therapy (ART)[1]. It has been widely shown that taking ART as prescribed staves off poor health outcomes through viral suppression in an HIV-positive population[2].

The success of ART depends on how well it is initiated, implemented and maintained[3]. Poor implementation, where there are delayed or missed doses, can impede viral suppression[4]. Although there are no agreed upon definitions of adherence in ART[5], studies have used measures that, depending on the medication being studied, range from 80% to 100% compliance[4]. A systematic review estimates that taking over 95% of medication as prescribed can lead to viral suppression[6].

Good adherence is important among HIV-positive pregnant women to prevent mother to child transmission (MTCT)[7]. A woman with an undetectable viral load is at a much smaller risk for MTCT in both the ante-[8] and post-natal periods[9]. Good health is closely related to good implementation of ART[7], and an adherent woman can decrease the frequency of secondary illnesses longer than a non-adherent woman, allowing her better quality of life and letting her care for her infant[10].

Adherence is an issue during pregnancy and into the post-partum period[11]. Women have been shown in some studies to have worse adherence to ART than men[12–14], and the new complications and stresses that come with pregnancy only add to this complex issue[6,15,16]. However, research on ART adherence among pregnant women is in the early stages[6,11] and still, little is known about the barriers pregnant women face in taking their medication.

Even less is known[6] about an emerging sub-group of this population[17]: women who do not initiate and then terminate ART with each pregnancy, but instead have persisted in taking lifelong ART regardless of pregnancy status. These women, who have conceived on ART, have been shown in a paper from the European Collaborative Study to have better personal health and healthier babies than women initiating ART during their pregnancy[8]. Because of the introduction of Option B+ parts of Southern Africa and around the world, which dictates that pregnant women persist on ART after delivery[18], this population of established users will only grow. With the adoption of Option B+ in the Western Cape, South Africa, this means that the landscape of HIV treatment in the country has changed. Due to the benefits of lifelong adherence, especially for mothers, and the lack of knowledge around this emerging group, it is important to describe the barriers to

adherence among HIV-positive pregnant women who have conceived on ART.

Methods:

As part of the Maternal and Child Health Antiretroviral Treatment (MCH-ART) study, a larger study of ART in pregnancy and into the postpartum period, a cross-sectional study of HIV-positive women in Gugulethu, Western Cape was conducted. This first phase consisted of a survey of women who presented for their first visit at a Midwife Obstetric Unit (MOU) in Gugulethu.

For inclusion in the study, women were over 18 years of age, pregnant (verified by ultrasound, urine test or clinical assessment) and were HIV-positive. Additionally, to be considered for this analysis, participants had to have been taking ART for at least four months to be considered on ART prior to conception. Participants were excluded if they were not pregnant or if they had a medical, physical or social condition that would preclude them from properly consenting to or participating in the study, such as denial of HIV status or refusal to take ART.

After abstraction from participant medical records to check ART status and duration, 502 participants from the original 1,544 were eligible for inclusion. During analysis, 16 participants were found to have missing questionnaire results and so were excluded from the analysis. However these participants were not significantly different from the rest of the sample with regard to the distribution of the outcome variable. The final sample size was 486.

Adherence was measured as the self-reported number of ART pills missed in the last 30 days. This was stratified into two groups for a binary outcome, comparing those who reported missing no doses in that time period to those who reported missing one or more doses. Self-reported measures of adherence are prone to bias, and in some studies have been shown to be unreliable[2]. To provide some measure of internal validity, the outcome measure was validated against other scale measures used in the study.

Seven assessments were used to measure possible confounders. The Demographics and Medical History assessment was created in-house to acquire basic demographic information, such as age and data used to create a variable for socio-economic status (SES). Information was also collected on previous ART use, hospitalisations and pregnancy.

The HIV Treatment Knowledge (HIV-TK) and the HIV/AIDS Knowledge Inventory (HIV-KI) both used true and false questions, with “Don't know” and “Refuse” options, to quantify participant's knowledge of the virus. The HIV-TK was adapted from Wagner et al.[19], and asked eight true and false questions to measure participant's understanding of how ART protects women along with their infants. The HIV-KI was adapted from Kalichman and Simbayi[20], and had three additional questions appended to the original: “Can a woman

give HIV/AIDS to her baby during breast feeding?"; "Does formula feeding reduce the risk of a baby getting HIV?" and "Do caesarean sections reduce the risk of a baby getting HIV?"

A composite score was generated for both sets of responses, with a point given for a correct response and no points given for an incorrect response or a refusal.

The other four questionnaires used scale assessments. The Beliefs About Medications Questionnaire (BMQ) was taken from the assessment from Horne et al.[21], and uses seven items from the original. It uses a five-item response scale, ranging from "Strongly Disagree" to "Strongly Agree," with an option for "Refuse." In the BMQ, participants were asked their opinions on statements about their medication's ability to keep them and their infant healthy. A composite score was generated for each participant, with the highest value of five given to the response expressing the strongest belief in the medication. There were no participants who refused to answer a question on this assessment.

The Adherence Self-Efficacy Scale (ASE), adapted from Chesney et al.[22], measured confidence and ability to adhere to medication during daily tasks, pregnancy and into the post-partum period. The scale used five items, with the lowest response being "Not confident at all," up to "Very confident." Again, a "Refuse" option was given. A composite score was calculated for each participant, with, again, the highest value of five for an answer of "Very Confident." There was one "Refuse" response, which was given the lowest response of one.

The London Measure of Unplanned Pregnancy (LMUP), adapted from Barrett et al.[23], uses six items to determine pregnancy intention. A composite score was generated for each participant. Items were scored according to the scoring guide provided in the original article's appendix[23], and analysed by its suggestion. To interpret: the lower the participant's LMUP score, the more unintended the pregnancy.

Maternal Adherence Assessment (MAA) was adapted from an article from Wilson et al.[24]. This assessment was used to measure medication side effects, adherence and reasons for non-adherence. A composite score was generated for adherence by adding up the following questions from this assessment: "Since you started taking them, how would you rate how well you usually do taking your HIV medicines in the way you are supposed to?" (Q8); "In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?" (Q11); "In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?" (Q12); "How hard is it for you to take your HIV medicines in a way you are supposed to?" (Q13). The highest value was assigned to the most desirable responses for each question, so that participants with the highest composite scores were self-reporting better ART adherence.

An analysis of the data was undertaken to describe the characteristics of study participants at

enrolment (see Table 1). A similar univariate analysis was conducted on the self-reported adherence measures used in this study (Table 2). A bivariate analysis was then conducted, comparing variables between those who reported missing no doses of their antiretrovirals in the last 30 days and those who reported missing one or more doses (Table 3). Categorical variables were compared using either chi-squared tests or Fisher's exact tests. Numerical variables were compared using two-sample t-tests and Wilcoxon Rank-sum tests. All comparisons used a 95% level of significance.

Cronbach's alpha was derived for each of the psychometric assessments (see Table 4; for a more detailed table, see journal article Appendix A). These six measures were previously validated; however alphas were calculated to assess their reliability with regard to this specific population. A cut-off of 0.7 was used and has generally been recognised as a good benchmark for internal consistency and reliability[25]. Scores from assessments with alphas below this cut-off were also used in model building, however a test does not need to approach a perfect scale to be interpretable[26] and scales with low inter-item correlations can still yield results.

A logistic regression model was built using variables identified in a review of the literature as possible confounders (see Table 5). Variables were organized into three categories: interpersonal, intrapersonal and background[16]. A prospective step-wise procedure was used to select the best-fitting model to describe the statistically significant barriers to adherence among this population.

The University of Cape Town’s Faculty of Health Sciences Human Research Ethics Committee gave ethical approval for this analysis.

Results:

Of the 486 HIV-positive pregnant women included in this analysis, all were African, 98% of participants spoke isiXhosa and the mean age was 31 years. Among participants, the matriculation prevalence was 22%, and 38% reported working either full-time or part-time. Using the responses for level of educational attainment, employment status, housing type and number of amenities in the household, a categorical variable was created for SES. The low SES bracket had 30% of participants; 36% of participants were in the middle bracket and 34% in the high bracket.

Almost all of participants reported currently being in a relationship (99%). The median length of relationships reported was four years, with 50% of participants who were in a relationship saying that they were married or living with their partner. The vast majority of participants reported disclosure of their status to at least one other person (99%), with 86% of those reporting having done so to their significant other.

Participants reported being on ART for a median of 3 years (IQR 1;5) and 58% of participants reported knowing the name of their medication. The median number of doses missed in the past 30 days was 0, though some participants reported missing up to 30 doses. One or more doses were missed by 22% of participants in the past 30 days.

The bivariate analysis showed a statistically significant difference between outcome groups with regards to SES category, with those reporting missing at least one dose in the past 30 days having a higher proportion of participants in the highest SES category compared to those who reported missing no doses (42% vs. 32%). Those who reported missing no doses had a statistically significant higher median score for medication belief (27.5 vs. 26), maternal adherence (19 vs. 17) and pregnancy intention (5.5 vs. 3). The ASE showed no difference in median score between the groups, however the lower limit for the IQR for those reporting missing no doses was higher and a rank-sum test showed a statistically significant difference between the two medians ([73;75] vs. [66.5;75]). Of those who missed no doses, 87% also reported disclosing their status to their male partner, compared to 79% of those who reported missing one or more doses.

Both the HIV-TK and the HIV-KI had low alphas, and so were poor measurement tools in this population (alpha=0.32; alpha=0.40, respectively; see Table 4). In both of these assessments, participants answered a high proportion of each question correctly. However, due to the low alphas, these assessments were found not to be reliable measures of HIV and ART knowledge in this population. The four other psychometric assessments used all had high alpha values and thus provided reliable measures in this population.

Table 5 has four panels, each fitting a model a different way to explore the relationship between adherence and the variables measured in this study. Panel 1 shows the unadjusted odds for each variable with respect to reporting no missed doses of ART in the past 30 days. Panel 2 reports the adjusted odds fitting age and SES category with each variable. Adjusting for age and SES did not appreciably change any of the odds when compared to the unadjusted odds in Panel 1. Panel 3 reports a model adjusting for age and SES, along with all of the scale assessments used in the study. In this panel, the ASE, HIV-KI and the HIV-TK all contributed insignificantly to the model's fitting of the outcome measure.

Panel 4 fits a full model including only variables that significantly contributed to improving the fit. A Hosmer and Lemeshow goodness-of-fit test showed the model to be an appropriate fit for the data (p=0.30). The largest effects were seen with SES category, maternal adherence and medication belief scores. For every one unit increase in maternal adherence score, a participant was 52% more likely to report missing no doses in the last 30 days. A higher SES was found to be harmful to ART adherence in this model, with those

in the middle and high SES brackets 59% and 66% less likely to report missing no doses in the past 30 days compared to those in the low SES bracket, respectively.

Discussion:

This study is one of the first in South Africa to examine adherence in HIV-infected women who conceive while established on ART. The principal objective was to determine the factors associated with adherence in order to identify risk factors in this understudied but important and growing population that may be amenable to intervention. The analysis suggests that adherence self-efficacy; medication beliefs and pregnancy intentions were associated with higher self-reported adherence.

Though they individually had small and statistically insignificant effects, the inclusion of self-efficacy and pregnancy intention in combination significantly improved the fit of the model, and their observed positive associations were in keeping with the literature. Self-efficacy has been previously shown to impact adherence[6,27], and has been acknowledged as an important step in affecting long-term change in health behaviour[28]. Pregnancy intention speaks to participants' fertility decisions and control over their reproductive health[29]. Those with scores indicating intended pregnancies were found to be more likely to not miss a dose, which might mean that these women are more efficacious or in situations that allow them more agency over their health behaviour.

It is a natural fit for participant's strong belief in their medication to affect their adherence, and previous studies have shown that those who feel that they need their medication and have faith in its ability to keep them healthy have better adherence than those with negative perceptions of their medication[6,19,21]. Horne et al. suggested that knowledge of the illness being treated by the medication might also affect adherence and be modified by medication belief[21]. This was not found to be true in this analysis, as neither HIV-TK nor HIV-KI scores were statistically significant variables in the model.

The association found in this model with SES, with those of low SES being more likely to report good adherence than those of middle and high SES, is counter to the literature, as low SES has previously been associated with poor adherence to ART[6,16,30]. In this study, participants in the lowest SES bracket were significantly more likely to report not currently being employed when compared to those in the mid and high brackets ($p<0.01$). One possibility in explaining this relationship is that the women who are employed have families who are dependent on them and are unable to afford to take time off work[16] to access health care.

The strongest association in the model was with maternal adherence score. This association, as well as the adherence assessment's strong internal consistency, speaks to the reliability of the self-reported measures in the study. A correlation matrix (see journal article Appendix B) showed a statistically significant

negative linear relationship between the number of missed doses reported by participants and how well they rated their adherence in a number of questions (rating adherence since initiation, in the last 30 days, etc.), though some of these correlations were weak. These correlations are interesting as they were all statistically significant, despite the fact that each measure used different measures of adherence or different time scales. It would be interesting for future research to further explore this topic, and to look at the correlation between measures using adjectival, adverbial and numerical scales in greater detail.

As this analysis was conducted with data drawn from a cross-sectional study, we cannot conclusively determine the causality of any of the factors significantly associated with the outcome in the model. For example, being of higher SES itself probably would not cause someone to be non-adherent to ART, though the association observed in this study might speak to some underlying factors in participants' lives that might affect their adherence, such as work schedules and issues with disclosure of status to employers[16]. It is easier to hypothesize that some factors in the model came before poor adherence, like medication belief and self-efficacy[22]. Another limitation of this analysis is that some risk factors for poor adherence to ART identified in the literature were not measured, like depression[1,11,31] and substance abuse[6,11,27]. Therefore their association with adherence cannot be adjusted for. There was some missing data, leading to the exclusion of 16 participants. Some of this loss was to allow ART duration to be used in model building as it has previously been shown to have significant associations with adherence[2,32], however it was statistically insignificant. Ultimately, participant viral load was not considered for this analysis, because viral load can be affected by details such as what line of treatment a participant is on and drug resistance[33], neither of which were measured in this part of the study. Future research into the association between viral load and adherence in the population could yield interesting results.

Finally, there is the issue of interpretation of these results. This article's strength, the emerging population studied, needs to be carefully defined and considered when looking at these results. Because this is such a unique group, the findings of this article should not be seen as transferable to other populations. This article speaks specifically to the barriers faced by women who are established on ART, HIV-positive and pregnant, and should not be stretched beyond those constraints. Further research should be done into adherence among male and non-pregnant female established users of ART to provide a complete picture of adherence patterns in the Western Cape and South Africa.

Keeping the above limitations in mind, there are a number of strengths for this study. The objectives of this research article address a critical gap in the literature on ART adherence[6]. It sheds some light on the factors that affect adherence among this group using tools that take less than 20 minutes to complete, are validated in this population and already translated into the local language, isiXhosa. The model built in this

analysis could have important future use with the expansion of ART delivery in the Western Cape due to the provincial health department's adoption of Option B+[18]. As this model has only a few significant variables, all of which can be measured speedily, this could be applied in a busy clinic setting to help identify poor adherers and provide additional support to encourage taking ART. With piloting to determine optimal cut-offs and sensitivity for a final composite score from the measurements, this model could become a useful tool for healthcare workers looking for a quick and easily interpretable assessment.

Enabling women to maintain their health and supporting them as they take their ART is of great importance to public health in South Africa. Achieving the World Health Organisation's goal of elimination of mother to child transmission by 2015 requires better adherence throughout the PMTCT cascade[12]. More research done into the barriers of adherence in pregnant women will make it easier for healthcare providers to identify potential non-adherers and to better support those on ART to reach this goal.

Acknowledgements

Thank you to Tammy Phillips and the rest of the MCH-ART study staff. Thank you to the National Institutes of Health for funding the MCH-ART study. Thank you to Prof. Landon Myer of the University of Cape Town for use of data from the MCH-ART study and for your guidance as my advisor.

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Tables

Table 1: Baseline characteristics of participants in study

Demographic Variables N=486		N (%)
Age	*Mean (Std)*	31 (5)
African Ethnicity		486 (100)
Home language	*isiXhosa*	476 (98)
Finished secondary school		105 (22)
Working		187 (38)
Household income from full time employment		282 (58)
Type of home		
	Shack/informal dwelling	282 (58)
	House/flat/hostel	204 (42)
SES category		
	Low	144 (30)
	Middle	177 (36)
	High	165 (34)
Median number of times pregnant (*IQR)*		3 (2;3)
LMUP category		
	Planned	131 (27)
	Ambivalent	126 (26)
	Unplanned	229 (47)
Currently in a relationship		480 (99)
	Married/cohabitating	240 (50)
Median length of relationship (IQR)		4 (2;8)
Current partner is the parent of any of your children		478 (100)
Mean number of family members disclosed to (std)		5 (3)
Told anyone that you were HIV positive		481 (99)
	Husband/partner/boyfriend	415 (86)
	Mother	271 (56)
	Sister	357 (74)
	Health professionals	481 (100)
	Friends	318 (66)
Median ART duration (years) (IQR)		3 (1;5)
Median number of missed doses in last 30 days (IQR)		0 (0;0)
	0	378 (78)
	1	34 (7)
	2	37 (8)
	3-10	31(7)
	30	6 (1)

Std, standard deviation; SES, Socio-economic status; LMUP, London Measure of Unplanned Pregnancy; ART, antiretroviral therapy; IQR, interquartile range

Table 2: Baseline ART and adherence characteristics of participants

Adherence measures N=486	N (%)
Know the name of their current ART regimen	283 (58)
Participants who have never stopped ART regimen	440 (91)
Since you started taking them, how would you rate how usually do taking your HIV medicines in the way you are supposed to?	
Poor or fair	20 (4)
Good	218 (45)
Very good	181 (37)
Excellent	67 (14)
Now think about the last 30 days. How would you rate how well you did taking your HIV medicines?	
Worse than usual	76 (16)
Better than usual	8 (2)
About the same as usual	402 (83)
How hard is it to take you medication as you are supposed to?	
Extremely or very hard	8 (2)
Somewhat hard	28 (6)
Not very hard	205 (42)
Not at all hard	245(50)
In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?	
Very poor or Poor	10 (2)
Fair	24 (5)
Good	182 (37)
Very good	182 (37)
Excellent	88 (18)
In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?	
Never, rarely or sometimes	16 (3)
Usually	165 (34)
Almost always	114 (23)
Always	191 (39)

ART, antiretroviral therapy

Table 3: Bivariate analysis of outcome measure and variables of interest

		Missed a dose in past 30 days (n=108) (22)	Has not missed a dose in past 30 days (n=378) (78)	P-value
Age mean (std)		31 (5)	31 (5)	0.54
SES score	*Low*	21 (19)	123 (33)	
	Middle	42 (39)	135 (36)	
	High	45 (42)	120 (32)	0.02
Finished high school		25 (23)	80 (21)	0.66
Median ASE score (IQR)		75 (66.5;75)	75 (73;75)	0.01
Median MBQ score (IQR)		26 (23;31)	27.5 (24;33)	<0.01
Median MAA composite score (IQR)		17 (15;19)	19 (17;21)	<0.01
Median HIV-KI score (IQR)		6 (5;7)	6 (5;7)	0.99
Media HIV-TK score (IQR)		7 (6;7)	7 (7;7)	0.24
LMUP score (IQR)		3 (1;9)	5.5 (3;10)	<0.01
LMUP Pregnancy Intention				
	Planned	20 (19)	111 (29)	
	Ambivalent	29 (27)	97 (26)	
	Unplanned	59 (55)	170 (45)	0.07
Know ART regimen		61 (56)	222 (59)	0.68
Median years on ART (IQR)		3 (1;5)	3 (2;5)	0.38
Disclosed HIV status		106 (98)	375 (99)	0.31
Median number of family members disclosed to (IQR)		4 (3;8)	4 (2;7)	0.39
Disclosure to male partner		85 (79)	330 (87)	0.04
Detectable (≥50 units) viral load		30 (28)	74 (20)	0.07

Std, standard deviation; SES, Socio-economic status; ASE, Adherence Self-efficacy Scale; IQR, interquartile range; BMQ, Beliefs About Medication Questionnaire; MAA, Maternal Adherence Assessment; HIV-KI, HIV/AIDS Knowledge Inventory; HIV-TK, HIV Treatment Knowledge Score; LMUP, London Measure of Unplanned Pregnancy; ART, antiretroviral therapy

Table 4: Cronbach's Alphas for Psychometric Scale Measures

Name of Scale	Cronbach's Alpha
Assessment of Self-efficacy	0.93
Beliefs About Medication Questionnaire	0.80
Maternal Adherence Assessment	0.84
London Measure of Unplanned Pregnancy	0.88
HIV Treatment Knowledge	0.32
HIV/Aids Knowledge Inventory	0.40

Table 5: Models predicting not missing a dose in the last 30 days

	Panel 1 (unadjusted)		Panel 2 (adjusted for age and SES)		Panel 3 (model of psychometric measures adjusted for age and SES)		Panel 4 (full model)	
	OR	CI	OR	CI	OR	CI	OR	CI
Sociodemographic Factors								
Age	1.01	(0.97;1.06)			1.00	(0.95;1.06)		
SES (vs. Low)	1	1			1	1	1	1
Middle	0.55	(0.31;0.98)			0.41	(0.21;0.81)	0.41	(0.21;0.81)
High	0.46	(0.26;0.81)			0.33	(0.17;0.66)	0.34	(0.17;0.68)
Finished secondary school	0.89	(0.53;1.49)	1.15	(0.66;2.02)				
Intrapersonal Factors								
ART duration (years)	1.03	(0.95;1.13)	1.03	(0.94;1.13)				
MBQ Score	1.07	(1.02;1.12)	1.07	(1.02;1.12)	1.16	(1.09;1.23)	1.17	(1.10;1.23)
ASE Score	1.04	(1.01;1.08)	1.05	(1.02;1.08)	1.03	(1.00;1.07)	1.03	(1.00;1.07)
MAA Score	1.35	(1.24;1.47)	1.36	(1.25;1.49)	1.52	(1.36;1.70)	1.52	(1.36;1.69)
LMUP Score	1.09	(1.03;1.15)	1.10	(1.03;1.16)	1.07	(1.00;1.14)	1.07	(1.00;1.14)
HIV-TK Score	1.20	(0.96;1.51)	1.20	(0.95;1.51)	1.11	(0.84;1.46)		
HIV-KI Score	1.02	(0.87;1.19)	1.04	(0.89;1.22)	1.07	(0.89;1.28)		
Interpersonal Factors								
Disclosed status to anyone	2.36	(0.39;14.30)	2.59	(0.42;16.07)				
Disclosed status to male partner	1.86	(1.07;3.22)	1.95	(1.11;3.42)				

SES, Socio-economic status; OR, odds ratio; CI, confidence interval; ART, antiretroviral therapy; BMQ, Beliefs About Medication Questionnaire; ASE, Adherence Self-efficacy Scale; MAA, Maternal Adherence Assessment; LMUP, London Measure of Unplanned Pregnancy; HIV-TK, HIV Treatment Knowledge Score; HIV-KI, HIV/AIDS Knowledge Inventory

Part D

Appendices

I. UCT Human Research Ethics Committee Study Approval Letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492 • **Facsimile** [021] 406 6411
Email: Sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

19 February 2015

HREC/REF: 057/2015

Prof L Myer
CIDER
School of Public Health and Family Medicine
FHS

Dear Prof Myer

Project Title: ADHERENCE IN HIV-POSITIVE WOMEN ENTERING ANTENATAL CARE ON ANTIRETROVIRAL THERAPY: A CROSS-SECTIONAL STUDY (Masters candidate-Briana O'Sullivan- LINKED TO 451/2012

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year until the 28 February 2016.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

We acknowledge that the following student:-Briana O' Sullivan is also involved in this project.

Please find the comments below for your benefit:-

- There are some limitations to the study: namely some data known to impact on adherence to ART has not been collected (e.g. depression, substance use details), and that the adherence outcomes available are all self-reports. However these limitation have been identified and discussed in the proposal. It would be interesting to use the objective viral load suppression data (drawn at the time of questionnaire in the parent study) as an outcome measure, as well as the subjective adherence data.

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence.

Hrec/ref:057/2015

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Hrec/ref:057/2015

II. Protocol Appendices

Appendix A

Phase 1 Informed Consent Form

TITLE OF RESEARCH: **Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study**

WHAT IS THE PURPOSE OF THIS STUDY?
We are from the University of Cape Town and ICAP at Columbia University. You are being asked to take part in a study that is being conducted at the Gugulethu Midwife Obstetric Unit (MOU). The purpose of this study is to understand how to improve health care services for HIV-positive women during their pregnancy and after they deliver the baby.

We know that it is important for their own health as well as the health of their baby, that HIV-positive women receive the HIV care and treatment that they need both during and after delivery. Information learned in this study will help us to improve HIV services for pregnant women.

You are being asked to take part in this study because you are a pregnant woman who is HIV-positive and you are getting your pregnancy care here at the Gugulethu MOU. The purpose of this consent is to give you information to help you decide if you want to take part in this study.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?
If you agree to take part, you will do the following at today's visit:

- Answer questions about your household, medical history, partnership status, HIV testing history and disclosure status , family planning and previous use of HIV drugs
    - If you are currently taking HIV drugs, we will ask you additional questions about HIV and HIV drugs (including side effects and adherence).
- Have 5mLs (1 teaspoon) of blood drawn from your arm)

NOTE: The blood that is drawn today will be stored and used to check your viral load (this is the amount of HIV in your blood) at a later time. Results from these tests will **not** be available to you, the clinic, or the study staff. When the health care providers at the clinic need to check your viral load, they will take a separate blood specimen. When it is stored, your blood and test results will not have your name or any other way of identifying you attached to it.

Review of medical records
As part of this study, we will also be looking at and taking information from your antenatal, obstetric, ART clinic, laboratory and pharmacy records. From these records, we are interested in learning about the pregnancy care you received as well as information about your delivery. We also want to learn about the HIV care and treatment that you received during your pregnancy and after you delivered. Finally, we want to learn about your baby's health status after delivery as well.

All data that we review and abstract is confidential and no participant names are recorded on study documents.
Contact for future study
After the completion of this visit, it is possible that we will contact you again at your next clinic visit or at another time in the future to take part in additional research studies. At that time, you would be asked to review and sign another consent form. You can choose to not take part in any future studies if you are asked. You will be asked to provide contact information so that we may get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

WHAT ARE THE POTENTIAL RISKS?
If you decide to participate, you may feel uncomfortable about some of the personal questions you are asked about your health or your pregnancy. You may refuse to answer any question that you do not want to answer. There is some risk in sharing personal and medical information. We will be careful to keep all your information as private as possible.

Drawing blood is normally done as part of routine medical care and presents a slight risk of discomfort. Experienced staff will draw blood under sterile conditions in order to protect you against these risks.

WHAT ARE THE POTENTIAL BENEFITS?
There is no direct benefit to you if you take part in this study but if we identify any health care problem during the course of the study, we will make sure you are referred to the appropriate health care services. The information gained in this study may help to improve ART services for HIV-infected pregnant women in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?
The alternative to taking part in this study is to continue with your usual care at the MOU.

WHAT ABOUT CONFIDENTIALITY?
If you agree to take part, all information collected during the study will be kept strictly confidential. Your name will not be written on the study forms and will not be used in connection with any information or lab specimens that are collected as part of the study.

All study materials will be stored in locked filing cabinets. Only study staff and personnel involved in routine audits will have access to these materials. All staff involved in data collection and management will get specific training in confidentiality.

Even with these procedures in place, if the study staff learns that you are a risk to yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

WILL I BE GIVEN ANYTHING FOR TAKING PART?
No, there is no compensation for taking part in the study today.

ARE THERE ANY COSTS?
There is no cost for being in this study.

CAN I LEAVE THE STUDY?
You have the right to decide not to not take part in the study, to refuse to answer any questions, or to withdraw from the study at any time without any penalty. It will have no effect on the care that you receive at the Gugulethu MOU or any other health facility.

FUTURE USE OF SPECIMENS:

If you agree, any leftover blood from the sample you have provided for this research project may be used for future HIV related research. It is possible that these stored samples may be tested to see if the HIV in your blood is resistant to any types of HIV medications or to look at other questions related to HIV.

At this time, we cannot provide details of when this testing may be conducted. However, additional testing will not be done using these stored samples without the approval of the appropriate ethics committees involved in this research.

If you agree to let us keep your stored samples for future research, they may be kept in a locked freezer for up to 5 years. If we do use your samples in the future, your name or other identifiers will not be included with this information (as with the rest of the information we collect for this study).

Please initial below to indicate whether or not you give permission for your specimens to be used for future research. You may still remain in the study, no matter which you choose.

_____ (initial) I agree to have my blood stored for future research.

_____ (initial) I agree to have my blood stored for future research related to this study ONLY.

_____ (initial) I do **NOT** agree to the storage of my blood for future research.

DO YOU HAVE ANY QUESTIONS?

If there is anything that is unclear or if you need further information, please ask us and we will provide it.

Do you have any questions?

FOR ADDITIONAL INFORMATION:

If you have any questions or have any problems while taking part in this research study, you should contact:

Dr Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences, University of Cape Town
Tel: 021 406 6661
Email: Landon.Myer@uct.ac.za

Dr Elaine Abrams
ICAP, Columbia University
Mailman School of Public Health
College of Physicians and Surgeons
Tel: +1 212 342 0543
Email: eja1@columbia.edu

If you have any questions about your rights as a research participant, you may contact the following member of the ethics committee:

Prof Marc Blockman
Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape

Columbia University Medical Center IRB
Tel: +1 212 305 5883

Town
Tel: 021 406 6338

CONSENT STATEMENT:

I have read this form, or someone has read it to me. I have been offered a copy of this consent form. I was encouraged and given time to ask questions. I agree to be in this study. I know that after choosing to be in this study, I may withdraw at any time. My being in the study is voluntary. I understand that whether or not I participate will not affect my health care services received today, or at any time in the future.

Please indicate your consent with your signature.

Volunteer's name _____

_____ _____
Signature of Volunteer Date

Staff member's name_____

_____ _____

Signature of study staff Date

If the volunteer is unable to read or write the entire counselling process must be observed by an independent witness who can then confirm the procedure once the she has given consent.

Fingerprint of volunteer:

Witness:
I confirm that I am independent of the study and that I witnessed the entire informed consent counselling process in the home language of the volunteer

Witness's name_____

_____ _____

Signature of witness Date

Thank you.

Appendix B

MCH-ART: Demographics & Medical History, Phase 1 PID: 1 - __ __ __ __ - __ __
Xhosa-English of Version 3.0, 15 October2013

		Visit Date: __ __/__ __ __/__ __ __ __
1.	Mingaphi iminyaka yakho *What is your age?*	*Age:* _____Iminyaka/*years*
2.	Ulohluphi uhlanga *What population group do you belong to?*	UmAfrika African = 1 Indiya *Indian* = 2 Umntu webala *Coloured* = 3 Umlungu *White* = 4 Olunye = 5, cacisa: _____ *Other specify*
3.	Uthetha oluphi ulwimi ekhayai? *What language do you speak at home?*	isiXhosa = 1 isiZulu = 2 isiBhulu *Afrikaans* = 3 isiNgesi *English* = 4 Olunye = 5, cacisa: _____ *Other specify*
4.	Lelephi elona banga liphezulu oliphumeleleyo? *What is the highest level of schooling/education that you have completed?*	Umgangatho/*Grade*:_____ Okanye/*or* Ibanga/ *Standard*:_____ Imfundo enomsila/ *Postsecondary*:_____
5.	Ngoku uyasebenza okanye uyafunda *Are you currently working and /or studying?*	Hayi *No* = 0 → Gqithela ku Q7 **SKIP to Q7** Ewe *Yes* = 1
6.	Ukuba nguEwe, yeyephi kwezi zilandelayo echaza, bhetele ukuba wenza ntoni? *If yes, which of one the following best describes what you do?* Khetha ibenye */Choose one only*	Ndiphangela isigxina = 1 *Employed full-time* Ndiphangela mangqaphangqapha = 2 *Employed part-time* Ndiphangela izingxungxo/ ndingumatheng 'ethengisa = 3 *Informal job/hawker* Uhamba isikolo/ ungumfundi = 4 *Attending school/learner* Uhamba isikolo semfundo enomsila = 5 *Attending tertiary education facility*
7.	Ngowuphi owona mthombo wemali kwikhaya lakho? *What is the MAJOR source of income for your household?* Khetha ibenye */Choose one only*	Ayikho =0 *None* Umsebenzi osisigxina =1 *Full-time employment* Umsebenzi wamaangqaoha-ngqapha =2 *Part-time employment* Umsebenzi wezingxungxo/ umthengisi =3 *Informal employment* Imali yesibonelelo sokukhuba zeka karhulumente= 4 *Disability grant* Imali yesibonelelo karhulumente =5 *Social grant* Umhlala phantsi =6 *Pension* Olunye imali yesibonelelo =7 *Other grant* chaza:_____ *specify type* Olunye =8 *Other* Chaza: _____ *specify* Andazi = 9 *Don't know*

Initials of counsellor: _____

8.	Uhlala kwikhaya elinjani? *What kind of home do you live in?*		Ityotyombe/ uhlaliso olungahlelwanga = 1 *Shack/informal dwelling* Indlu yesitena = 2 *Formal house* Ifleti/ indlu kamaspala = 3 *Flat/council home* Enye = 4, chaza:_____ *Other, specify*
9.	Ingaba indlu yakho inazo ezi zinto zilandelayo: *Does your house have the following: Read and answer for all*	a. Indlu yangasese *A toilet inside*	Hayi/*No* =0 Ewe/*Yes* =1
		b. Amanzi abalekayo empompo *Running water inside*	Hayi/*No* =0 Ewe/*Yes* =1
		c. Umbane *Electricity inside*	Hayi/*No* =0 Ewe/*Yes* =1
		d. Isikhenkcisi *A refrigerator*	Hayi/*No* =0 Ewe/*Yes* =1
		e. Umnxeba *A telephone*	Hayi/*No* =0 Ewe/*Yes* =1
		f. Umabona kude *A television*	Hayi/*No* =0 Ewe/*Yes* =1
10.	Bangaphi abantu abahlala kule ndlu bedibene nawe(abadala,abancinci)? *Including yourself, how many people (adults and children) live in your house?*		Inani labantu: _____ # *of people:*
11.	Bangaphi abadala (iminyaka-16 nangaphezulu)bedibene nawe abahlala kule ndlu? *How many adults (aged 16 or older), including you, live in your house?*		Inani labadala:_____ # *of adults*
12.	Bangaphi abantwana (iminyaka -15 nanganeno) abahlala nawe? *How many children (aged 15 and under) live in your house?*		Inani labantwana:_____ # *of children*
13.	Ukhulelwe kangaphi (kudibene nesi isisu)? *How many times have you been pregnant (including current pregnancy)?*		inani lokukhulelwa: _____ # *of pregnancies:*
14.	Ingaba ubuzama ukuba nosana ngelixesha ufumanisa ukuba ukhulelwe (Kwesi isisu)? *Were you trying to have a baby when you found out you were pregnant (in this pregnancy)?*		Hayi/*No* = 0 Ewe/*Yes* = 1 Andazi/*I don't know* = 9
15.	Bangaphi abantwana obazeleyo? *How many children have you given birth to?*		Inani labantwana:_____ # *of children* **Ukuba = 0,** Gqithela ku Q20 ***If 0, SKIP to Q20***
16.	Bangaphi kwaba bantwana abaphilayo? *How many of these children are living?*		Inani labantwana:_____ # *of children*
17.	Bangaphi kwaba bantwana abahlala nawe ngoku? *How many of these children currently live with you?*		Inani labantwana:_____ # *of children*
18.	Bangaphi kwaba bantwana ekufumaniseke bakho ukuba baphila nentsholongwane? *How many of your children have tested HIV-positive?*		Inani labantwana abaphila nentsholongwane:_____ # *of HIV-positive children*
19.	Bangaphi kwaba bantwana baphila nentsholongwane abasaphilayo? *How many of these children who have tested HIV- positive are currently living?*		Inani labantwana abaphila nentsholongwane abaphilayo ngoku: _____ # *of HIV-positive children currently alive*

Initials of counsellor: _____

20.	Uya thandana ngoku? *Are you currently in a relationship?*	Hayi/*No* = 0→ **Gqithela ku Q25** ***SKIP to Q25*** Ewe/*Yes*= 1
21.	Ungaluchaza njani uthando lwakho*?* *How would you describe your current relationship?*	Utshatile = 1 *Married* Anditshatanga ,ndiya hlalisana =2 *Not married, living together* Nditshatile, asihlali kunye = 3 *Married, not living together* Anditshatanga, asihlali kunye = 4 *Not married, not living together* Enye = 5, cacisa:_____ *Other, specify*
22.	Lileshe ellingakanani unobudlelwana nalomntu? *How long have you been in a relationship with this person?*	Ixesha Inyanga *Months*_____ *Duration in:* Iminyaka *Years*_____
23.	Ingaba eli qabane lakho ngutata womnye wabantwana bakho(kunye nalo umkhulelweyo)? *Is your current partner the parent of any of your children? (including current pregnancy)*	Hayi/*No* = 0 Ewe/*Yes* = 1
24.	Ulichazele na iqabane lakho ngesimo sakho sentsholongwane? *Have you disclosed your HIV status to your current partner?*	Hayi/*No* = 0 Ewe/*Yes* = 1
25.	Ubukhe wabelana ngesondo nabanye abantu ingenguye lomntu uthandana naye? *In the last 12 months have you had any sexual relationships/sexual partners? (if in a relationship then other than this partner)*	Hayi/*No* = 0 → **Gqithela ku Q28** ***→ SKIP to Q 28*** Ewe/*Yes* = 1
26.	Bunjani ubudlelwanebakho namanye amaqabane ngaphandle kweqabane lakho langoku ukuba akhona? *What is the nature of your relationship(s)? (other than current partner if applicable)* Rhangqa konke okungqamene nawe. *Mark all that apply.*	a. Umlingane/nditshatile *Spouse/ married* b. Iqabane lam *Boyfriend* c. Iqabane lethutyana *Casual Partner/One Night Stands* d. Omnye ,cacisa:_____ *Other, specify*
27.	Ubaxelele aba bantu wabelana nabo ngesondo ukuba uphila nentsholongwane? *Have you disclosed your HIV status to any of these other sexual partners?*	Hayi/*No* = 0 Ewe/*Yes* = 1
28.	Ubuqala ukufumanisa ukuba unentsholongwa kagawulayo kolumitho okanye phambi kokuba ukhulelwe? *Did you first test HIV positive <u>in this pregnancy</u> or <u>before this pregnancy</u>?*	Koku ukukhulelwa =1 → Gqithela ku Q32 *In his pregnancy* ***SKIP to Q32*** Phambi koku ukukhulelwa =2 *Before this pregnancy*
29.	Kwakunini ukuqala kwakho ukufumanisa ukuba unentsholongwane kagawulayo? *When did you 1st test HIV-positive?*	Umhla:___ Inyanga:_____ Unyaka:_____ Day Month Year
30.	Kwakutheni ukuze oluhlolo lwenziwe? *Why was this test conducted?*	Ndivavanywe ngelixesha ndikhulelweyo = 1 *Tested during pregnancy* VCT/Ndandifuna ukuvavanywe =2 *VCT/Wanted to be tested* Ndafunyaniswa ndinesifo sephepha (TB) = 3 *Diagnosed with TB* Ndangeniswa esibhedlele = 4 *Admitted to the hospital* Enye = 5, cacisa:_____ *Other, specify*

Initials of counsellor: _____

31.	Ingaba wawukhulelwe ukuqala kwakho ukufumane ukuba unentsholongwane kagawulayo? *Were you pregnant when you first tested HIV-positive?*	Hayi/*No* = 0 Ewe/*Yes* = 1
32.	Wakhe wanazo iziphumo ezingena chaphaza kuvavanyo lwentsholongwane kagawulayo? *Have you ever tested negative on an HIV test?*	Hayi/*No* = 0 →Gqithela ku Q36 ***SKIP to Q36*** Ewe/*Yes* = 1
33.	Ugqibele nini ukuba neziphumo ezingenachaphaza zovavanyo lwentsholongwane kagawulayo? *When did you last test HIV-negative?*	Umhla:___ Inyanga:_____ Unyaka:_____ Day Month Year
34.	Kwakutheni ukuze uvavanywe ngelo xesha? What was the reason for you doing the HIV test? *Why did you test at that time?*	Ndivavanywe ngelixesha ndikhulelweyo = 1 *Tested during pregnancy* VCT/Ndandifuna ukuvavanywe =2 *VCT/Wanted to be tested* Ndafunyaniswa ndinesifo sephepha (TB) = 3 *Diagnosed with TB* Ndangeniswa esibhedlele = 4 *Admitted to the hospital* Enye = 5, cacisa:_____ *Other, specify*
35.	Wawukhulelwe ngeloxesha uvavanyelwa intsholongwane? *Were you pregnant at the time of that test?*	Hayi/*No* = 0 Ewe/*Yes* = 1
36.	Wakhe waxelela nabanina ukuba unentsholongwane kagawulayo? *Have you told <u>anyone</u> that you are HIV-positive?*	Hayi/*No* = 0 →Gqithela ku Q39 ***SKIP to Q39*** Ewe/*Yes* = 1
37.	Ngawaphi amlungu osapho lwakho owaxeleleyo ngesimo sakho sentsholonwane? *Which of your family members have you told about your HIV status?* Nceda phendula lombuzo ngelungu ngalinye losapho oludweliswe ngezantsi. *Please answer this question for each of the family members listed below.* Wamxelele u_ _ _ _ _ _ _ ukuba unentsholongwane kagawulayo? *Have you told your _____ that you are HIV positive?*	
a.	Umyeni*/iqabane* *Husband/partner/boyfriend*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
b.	Umama *Mother*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
c.	Utata *Father*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
d.	Udade *Sister*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
e.	Umtakwenu *Brother*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
f.	Intombi *Daughter*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
g.	Unyana *Son*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
h.	Umalume *Uncle*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
i.	U-anti *Aunt*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9

Initials of counsellor: _____

j.	Umza wesikhomo *Male cousin*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
k.	Umza wesikhomokazi *Female cousin*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
l.	Enye indoda yalapha *Other male family member*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
m.	Esinye isikhomokazi *Other female family member*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
38.	Ngaphandle kwabantu bakowenu aba badweliswe ngentla,ngubani omnye umntu owamxelelyo ukuba uphila nentsholongwane?(funda uphendule yonke imibuzo) *Aside from family members listed above, who else have you told about your HIV status? (read and answer for all)*	
a.	Amanesi/ogqira *Health professionals*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
b.	Iqumru lenxaso labantu abaphila nentsholongwane *Support group*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
c.	Umntu owabelana naye ngesondo ongahlali naye *A sexual partner who does not live with you*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
d.	Isihlobo *Friends*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
e.	Inkokheli ngokwa kwamoya *Spiritual leader*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
f.	Umntu okuqashileyo/wayekuqashile *Current or former employer*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
g.	Ukuchaza esidlangalaleni *Public disclosure/ community*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
h.	Abanye, chaza: _____ *Other, specify*	Hayi/*No* = 0 Ewe/*Yes* = 1 N/A = 9
39.	Wakhe wakhulelwa phambi koku ukukhulelwa? *Have you ever been pregnant before this pregnancy?*	Hayi/*No* = 0 →Gqithela ku Q45 ***SKIP to Q45*** Ewe/*Yes* = 1
40.	Ngokuya ubukhulelwe ngaphambi koku ukukhulelwa wawuke wanikwa amayeza okhusela usana lungosuleleki yintsholongwane (ezeku khusela umntwana hayi amachiza okutho malalisa intsholongwane wobomi bonke) *When you were pregnant before this pregnancy have you ever been given medication at the clinic to keep your baby from getting HIV infected? (prophylaxis NOT lifelong ART)*	Hayi/*No* = 0 →Gqithela ku Q45 ***SKIP to Q45*** Ewe/*Yes* = 1
41.	Ukuba nguEwe, zingaphi izisu ufumane la machiza ngesisizathu? *If yes, during how many pregnancies have you received medication for this purpose?*	Inani lezisu:_____ *# of pregnancies*

Initials of counsellor: _____

42.	Kwezi zisu siyi____ofumene kuzo amachiza, zingaphi izisu otye kuzo iipilisi ngelixesha ubelekayo qha? *For the ___ pregnancies that you received medication, For how many pregnancies did you take pills while you were pregnant and for how many pregnancies did you take pills only at delivery?*	Ngoku wawubeleka *Only at Delivery (Nevirapine) #:*_____ Ngelixesha ukhulelwe *While you were pregnant (AZT)? #:* _____
43.	Bekunini ukugqibela kwakho ukufumana la machiza ngesisizathu? *When was the last time that you received medication for this purpose?*	Umhla:___ Inyanga:_____ Unyaka:_____ Day Month Year
44.	Uwafumene phi la machiza ukugqibela kwakho? *Where did you receive the medication the last time?*	Igama lekliniki:_____ *Name of clinic:*
45.	Wawuke wawathatha amachiza okuthomalalisa intsholongwane (awobomi bakho bonke) *Have you ever taken triple drug antiretroviral therapy (lifelong ART)?*	Hayi/*No* = 0 → Skip to Q51 Ewe/*Yes* = 1
46.	Ukuba nguEwe, ingaba wawafumana amachiza okuthomalalisa intsholongwane ukugqibela kakho? *If yes, where did you receive ART the last time?*	Igama lekliniki:_____ *Name of clinic:*
47.	Uqale nini ukutya la machiza okuthomalalisa intsholongwane kagawulayo? *When did you start taking ART?*	Umhla:___ Inyanga:_____ Unyaka:_____ Day Month Year
48.	Usawatya amachiza okuthomalalisa intsholongwane kagawulayo? *Are you still on ART?*	Hayi/*No* = 0 Ewe/*Yes* = 1→ SKIP to Q51
49.	Ukuba nguHayi,uyeke nini ukuwatya amachiza okuthomalalisa intsholongwane kagawulayo? *If No, when did you stop taking ART?*	Umhla:___ Inyanga:_____ Unyaka:_____ Day Month Year

Initials of counsellor: _____

50.	Uyekele ntoni ukutya amachiza athomalalisa intsholongwane? *Why did you stop taking ART?* (rhagqa zonke ezibhekisa kuwe) *Circle all that apply*	a. Ndaphelelwa ngumchiza andaya ukuyakuwalanda *I ran out of medicine and didn't go for refills* b. Anencasa embi *The medicine tastes bad* c. Ndulibala *I just forgot* d. Bendikhathazwa yimiphumela yawo *I was worried about the side effects* e. Bendingafuni abanye bandiqaphele ukuba nditya amachiza *I did not want others to notice me taking the medicine* f. Ndandigula *I was ill* g. Ndacinga ukuba andisawafuni nganto *Didn't think I needed it anymore* h. Bendicinga ndingahlala ndiphilile ngaphandle kwawo *Can stay healthy without it* i. Bendicinga ukuba lamayeza anganobu ngozi kum. *I felt the medicine might be harmful to me* j. Ndizive ndinoxinizelelo *I felt depressed* k. Ndandiphilile *I was well* l. Ebemaninzi la machiza ekufuneka ndiwathathe *There was too much medicine to take* m. Bendingekho ekhaya *I was away from home* n. Bendixakekile zezinye izinto *I was busy with other things* o. Ndiye ndafunda ukuba zikho ezinye iindlela endinganyanga okanye ndiphilise intsholongwane kagawulayo *I learned that there are other ways to treat or cure HIV* p. Enye, cacisa: _____ *Other, Specify*
51.	Ubukhe watshaya isagarethi kulenyanga iphelileyo? *Did you smoke cigarettes in the last month?*	Hayi *No* = 0 → END Ewe *Yes* = 1
52.	Utshaya isigarethi ezingaphi ngemini? *How many cigarettes do you smoke in a day?*	#_____ cigarettes

Date completed: _ _ /_ _ _ / _ _ _ _ Signed counsellor completing CRF: _____

Date of QC: _ _ /_ _ _ / _ _ _ _ Signed measurement nurse: _____

Initials of counsellor: _____

Appendix C

MCH-ART: HIV/AIDS Treatment Knowledge Inventory Phase 2 1st visit PID: 2 - __ __ __ __ - __ __
Xhosa-English Version 2.1, 28 Jan 2013

HIV/AIDS TREATMENT KNOWLEDGE INVENTORY Visit Date: __ __/__ __ __/__ __ __ __

Le mibuzo ilandelayo ifuna ulwazi lwakho ngonyango lwe HIV/AIDS. Nceda utsho ukuba "kunjalo," "bakunjalo," okanye "andazi." Ukuba akuyazi, nceda uthi "andazi" endaweni yokuqatshisa ukuba "kuyinyani," okanye "akuyonyani."
The next questions ask about your knowledge of HIV/AIDS treatments. Please answer "true," or "false." If you don't know the answer to a question, please answer "don't know" instead of guessing "true" or "false." Indicate by circling your answer for each statement.

		Kunjalo *True*	Akunjalo *False*	Andazi *Don't know*	Ndiyala *Refuse*
1	"Indibanisela yonyango oluthathwa ngaxesha nye" lujolise ekuhliseninoksnye ekuthothiseni ukusebenza kwentsholongwane ye HIV virus emzimbeni. *Antiretroviral medication aims to reduce or suppress the activity of the HIV virus in the body.*	1	2	3	9
2	Ukuthatha indibanisela yonyango oluthathwa ngaxesha nye ngexesha kunceda ekugcineni izinga elifanelekileyo lamayeza emzimbeni womntu. *Taking antiretroviral medications on schedule helps keep the right amount of medicine in one's system.*	1	2	3	9
3	Umthwalo wentsholongwane (viral load) ngumlinganiselo wobungakanani bentsholongwane ye HIV egazini. *Viral load measures the amount of HIV virus in the blood.*	1	2	3	9
4	Ngamanye amaxesha iziphumo zegazi zibuya zisithi "AYIBONAKALI" intsholongwane,le nto ithetha ukuba ayikho intsholongwane eshiyekileyo *Sometimes lab results say that a person's viral load is "undetectable." This means that there is no virus left.*	1	2	3	9
5	Ukuthatha amachiza [iARVs] ngokomuyalelo lingathomalalisa izinga lentsholongwane. *Taking antiretroviral therapy exactly as prescribed is likely to reduce viral load.*	1	2	3	9
6	Ukutya amachiza athomalalisa intsholongwane kucutha amathuba wokuba usana lungasuleleki ngelixesha umama ekhulelwe naxa usana luzalwa. *Taking antiretroviral therapy can reduce a child's risk of becoming HIV infected during pregnancy and delivery.*	1	2	3	9
7	Ukutya amchiza athomalalisa intsholongwane icutha ukuba usana lingosulelwa xa lincanciswa ibele *Taking antiretroviral therapy can reduce a child's risk of becoming HIV infected during breastfeeding.*	1	2	3	9
8	Ukuba umntu otya amachiza athomalalisa intsholongwane ibe intsholongwane yakhe isazantsi,amathuba okusulela ngentsholongwane xa bebelana ngesondo nomntu ongaphili nentsholongwana mancinci. *If a person takes antiretroviral therapy and has a low viral load, they may be less likely to transmit the virus through having sex with an HIV-negative partner.*	1	2	3	9

Date completed: __ __ /__ __ __ / __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __ /__ __ __ / __ __ __ __ Signed measurement nurse: _____

Initials of counsellor

Appendix D

MCH-ART: HIV/AIDS Knowledge Inventory Phase 2 1st visit PID: 2 - __ __ __ __ - __ __
Xhosa-English Version 2.0, 28 Jan 2013

HIV/AIDS KNOWLEDGE INVENTORY Visit Date: __ __/__ __ __/__ __ __ __

Apha sinika inkcazelo nge HIV&AIDs. Kwenkcazelo nganye rhangqa impendulo okholelwa ukuba ilungile.
We are now going to ask you some questions about HIV/AIDS. For each one, tell me if you think the question is correct (Yes) or not (No).

		Hayi *No*	Ewe *Yes*	Andiyazi *Don't Know*	Ndiyala *Refuse*
1.	Ingaba intsholongwane kagawulayo isasa zeka ngokuncamisana? *Is HIV/AIDS spread by kissing?*	1	2	3	9
2.	Ingaba kufuneka umntu abena maqabane amaninzi ukuze osuleleke intsholongwane kagawulayo? *Must a person have many different partners to get HIV/AIDS?*	1	2	3	9
3.	Ingaba umama okhulelweyo angamosulela umntwana na wakhe ngentsholongwane kagawulayo? *Can a pregnant woman give HIV/AIDS to her baby?*	1	2	3	9
4.	Ingaba Ihiv intsholongwane ebangela ugawulayo *Is HIV the virus that causes AIDS?*	1	2	3	9
5.	Ingaba likhona iyeza elinyanga intsholongwane kagawulayo? *Is there a cure for HIV/AIDS?*	1	2	3	9
6.	Ingaba akhona amachiza angathathwa ngumama ukukhusela usana kwintsholongwane? *Are there medications that a woman can take to protect her baby from getting HIV/AIDS?*	1	2	3	9
7.	Ingaba umama angamosulela umntwana nge intsholongwane kagawulayo xa emncancisa ibele? *Can a woman give HIV/AIDS to her baby during breast feeding?*	1	2	3	9
8.	Ingaba ukuncancisa usana ubisi oluthengiweyo lucutha umngcipheko wosana kukosulelwa yintsholongwane? *Does formula feeding reduce the risk of a baby getting HIV?*	1	2	3	9
9.	Ingaba ukubelaka umntwana ngoqhaqho incutha umngcipheko wokosulela umntwana ngentsholongwane? *Do caesarian sections reduce the risk of a baby getting HIV?*	1	2	3	9

Date completed: _ _ /_ _ _ / _ _ _ _ Signed counsellor completing CRF: _____

Date of QC: _ _ /_ _ _ / _ _ _ _ Signed measurement nurse: _____

Appendix E

MCH-ART: Adherence Self-efficacy Phase 2 1st visit
Xhosa-English Version 2.1, 26 Jan 2013

PID: 2 - __ __ __ __ - __ __

ADHERENCE SELF-EFFICACY Visit Date: __ __/__ __ __/__ __ __ __

Kolu luhlu lulandelayo lwemibuzo, siza kuthi sikucele ukuba usixelele ukuba uqiniseke kangakanani ukuba ngokwazi ukuzithatha kakuhle amayeza akho kwiimeko nganye kwezi zidwelisiweyo. Nceda uphendule le mibuzo ilandelayo usebenzisa umlinganiselo 0 -5; ungakhetha naliphi na inani ukusuka ku 0 ukuya ku 5. u 1 uthetha ukuthi akuqinisekanga konke; u 3 uthetha ukuthi uqinisekile nje kancinci; u 5 uthetha ukuthi uqinisekile ngokupheleleyo.
In the next set of questions, please tell us how confident you feel that you can take your medications during each of the situations listed. Please answer using a 1 – 5 scale, where "1" means you are not at all confident, "3" means you are moderately confident, and "5" means you are completely confident. You can choose any number from 1 to 5.

Uqiniseke kangakanani ukuba uza kubambelela kwinkqubo yee amayeza akho.....
How confident are you that you can stick to your medication schedule…

		How confident →					
		uthetha ukuthi akuqinisekanga konke *Not confident at all*	**uthetha kuthi uqinisekile nje kancinci** *Moderately confident*			**uthetha ukuthi uqinisekile ngokupheleleyo** *Very confident*	**Ndiyala** *Refuse*
1.	Xa inkqubo yakho yemihla ngemihla iza kuphazamiseka? *When your daily routine is disrupted?*	1	2	3	4	5	9
2.	Xa imiphumela yazo iqala ukuphazamisana nemisebenzi yakho ye mihlangemihla? *When the side effects begin to interfere with your daily activities?*	1	2	3	4	5	9
3.	Xa kuyimpela veki? *On the weekends?*	1	2	3	4	5	9
4.	Xa uxakekile? *When you are busy?*	1	2	3	4	5	9
5.	Xa udiniwe? *When you are tired?*	1	2	3	4	5	9
6.	Xa umzimba wakho uphantsi okanye udakumbile? *When you are down or depressed?*	1	2	3	4	5	9
7.	Xa uziva uphilile? *When you are feeling healthy?*	1	2	3	4	5	9

Initials of counsellor

8.	Xa uziva ugula? *When you are feeling sick?*	1	2	3	4	5	9
9.	Xa usele utywala? *When you drink alcohol?*	1	2	3	4	5	9
10.	Xa ungafuni kukhunjuzwa nge HIV/AIDs? *When you don't want to be reminded about HIV/AIDS?*	1	2	3	4	5	9
11.	Xa kuthetha ukuthatha amayeza phambi kwabantu abangakwaziyo ukuba uphila ne ntsholongwane kagawulayo? *When it means taking your medications in front of people who don't know you are HIV+?*	1	2	3	4	5	9
12.	Xa uziva ugula kuba ukhulelwe? *When you are feeling sick from your pregnancy?*	1	2	3	4	5	9
13.	Xa uthatha unakekelo losana lwakho? *When you are busy taking care of your baby?*	1	2	3	4	5	9
14.	Xa uncancisa usana ibele? *When you are breast feeding your baby?*	1	2	3	4	5	9
15.	Xa uziva udiniwe ukuvuka nosana lwakho? *When you are tired from waking up with your baby?*	1	2	3	4	5	9
		uthetha ukuthi akuqinisekanga konke *Not confident at all*		**uthetha kuthi uqinisekile nje kancinci** *Moderately confident*		**uthetha ukuthi uqinisekile ngokupheleleyo** *Very confident*	**Ndiyala** *Refuse*

Date completed: __ __ /__ __ __ / __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __ /__ __ __ / __ __ __ __ Signed measurement nurse: _____

Appendix F

MCH-ART: ART Medication Beliefs Phase 2 1st visit PID: 2 - __ __ __ __ - __ __
Xhosa-English Version 2.1, 26 Jan 2013

BELIEFS ABOUT MEDICATIONS Visit Date: __ __/__ __ __/__ __ __ __

Imibuzo elendelayo iquka ulwazi lwako malunga namachiza e ntsholongwane kagaulayo. Nceda ubonise ukuba yeyiphi ovumelana okanye ongavumelani nayo kwezi ntetha zilandelayo "1" bonisa ukuba uvumelana kakulu kwaye "5" bonisa ukuba awuvumalani kakhulu.
The following questions involve your personal views about HIV/AIDS medications. Please indicate the extent to which you agree or disagree with the following statements. "1" indicates that you strongly disagree and "5" indicates that you strongly agree.

		Andivumi konke *Strongly Disagree*	**Andivumi** *Disagree*	**Andiqini-sekanga** *Uncertain*	**Ndiyavuma** *Agree*	**Ndiyavuma ngamandla** *Strongly Agree*	**Ndiyala** *Refuse*
1	Impilo yam ngelixesha ndikhulelwe ixhomekeke kumachiza wam *My health during my pregnancy depends on my medicines*	1	2	3	4	5	9
2	Impilo yosana ixhomekeke kumachiza endiwatyayo *My baby's health depends on my medicines*	1	2	3	4	5	9
3	Ukuthatha amachiza ngelixesha ndikhulelwe iyandikhathaza loo nto *Having to take medicines during my pregnancy worries me*	1	2	3	4	5	9
4	Iyandikhathaza into yokutya amachiza xa ndincancisa *Having to take medicines while I am breastfeeding worries me*	1	2	3	4	5	9
5	Ngaphandle kwamachiza andizukubanakho ukunakekela usana lwam *Without my medicines I will be unable to care for my baby*	1	2	3	4	5	9
6	Ngamanye amxesha ndiya khathazeka ngemiphumela yamachiza yexesha elide kusana lwam *I sometimes worry about the long-term effects of my medicines on my baby*	1	2	3	4	5	9
7	Xa ndincancisa amachiza am aza kukhusela usana lwam kwintsholongwane *When I am breast feeding my medicines will protect my baby from HIV*	1	2	3	4	5	9

Date completed: __ __ /__ __ __ / __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __ /__ __ __ / __ __ __ __ Signed measurement nurse: _____

Initials of counsellor

Appendix G

MCH-ART: The London Measure of Unplanned Pregnancy (LMUP) PID: 1-__ __ __ __-__ __
X-E Version 1.0 17 May 201

	Umhla Wotyelelo *Visit Date*	_ _ / _ _ _ / _ _ _ _ DD / MMM / YYYY
	Ngezantsi kunemibuzo ebuza ngemeko kunye nezimvo zakho ngeli xesha umithe. Nceda cinga ngolu mitho lwangoku xa uphendula lemibuzo ingezantsi. *Below are some questions that ask about your circumstances and feelings around the time you became pregnant. Please think of your current pregnancy when answering the questions below.*	
1.	Kwinyanga endimithe ngayo…. *In the month that I became pregnant.....* ***(Nceda tikisha intetha engqamelene nawe kakhulu):*** *(Please tick the statement which most applies to you):*	1. Mna/besingalu sebenzisi ucwangciso. *I/we were not using contraception* 2. Mna/besilusebenzisa ucwangcisa, kodwa hayi lonke ixesha *I/we were using contraception, but not on every occasion* 3. Mna/besilusebenzisa rhoqo ucwangciso, kodwa sisazi ukuba uhlobo alusebenzi(igqabhukile, ishenxile, iphumile, iphumile ngaphandle, ayisebenzi) kwankanje nje. *I/we always used contraception, but knew that the method had failed (i.e. broke, moved, came off, came out, not worked etc) at least once* 4. Mna/besilusebenzisa rhoqo ucwangciso. *I/we always used contraception*
5.	Kwindima yokuba ngumama(okokuqala, okanye ndiphinde) ndiziva ukuba umitho lwenzeke. *In terms of becoming a mother (first time or again), I feel that my pregnancy happened at the.....* ***(Nceda tikisha intetha engqamelene nawe kakhulu):*** *(Please tick the statement which most applies to you):*	1. Lixesha elilungileyo *right time* 2. ok, kodwa ayilo xesha elulingileyo *ok, but not quite right time* 3. lixesha elingalunganga *wrong time*
4.	Nje phambi kokuba ndimithe…. *Just before I became pregnant.....* ***(Nceda tikisha intetha engqamelene nawe kakhulu):*** *(Please tick the statement which most applies to you):*	1. Bendizimisela ukumitha *I intended to get pregnant* 2. Lingcinge zam bezintshentsho *my intentions kept changing* 3. Bendingazimisele ukumitha *I did not intend to get pregnant*
4.	Nje phambi kokuba ndimithe…. *Just before I became pregnant....* ***(Nceda tikisha intetha engqamelene nawe kakhulu):*** *(Please tick the statement which most applies to you)*	1. Bendifuna ukuba nosana *I wanted to have a baby* 2. Imizwa yam ibibethabethana ngokuba nosana *I had mixed feelings about having a baby* 3. Bendingafuni ukuba nomtwana *I did not want to have a baby*
4.	Phambe kokuba ndimithe… *Before I became pregnant....* ***(Nceda tikisha intetha engqamelene nawe kakhulu):*** *(Please tick the statement which most applies to you)*	1. Iqabane lam, nam sivumelene ukuba ndimithe *My partner and I had agreed that we would like me to be pregnant* 2. Iqabane lam, nam sixotile ukuba sibenabantwana sobabini kodwa asavumelana ukuba mna ndimithe *My partner and I had discussed having children together, but hadn't agreed for me to get pregnant* 3. Asikhange sixoxe ngokuba nabantwana sobabini *We never discussed having children together*
4.	Phambi kokuba imithe, ikho into oyenzileleyo ukuphucula impilo yakho ulungiselela umitho? *Before you became pregnant, did you do anything to improve your health in preparation for pregnancy?* ***(Nceda tikisha zonke engqamelene nawe)*** *(Please tick all that apply)*	a. Nditye iFolic Acid *took folic acid* b. Ndiyekile okanye ndabuyise unyawo ekutshayeni *stopped or cut down smoking* c. Ndiyekile okanye ndabuyise unyawo ekuseleni *stopped or cut down drinking alcohol* d. Nditye ukutya okusempilweni *ate more healthily* e. Ndiye ndafuna amacebisa empilo *sought medical/health advice* f. Ndiye ndathethe amanje amanyathelo nceda chaze: *took some other action, please describe:* _____ Okanye*/or* g. Akukho nenye endiyenzileyo kwezi zisentla phambi ndimithe *I did not do any of the above before my pregnancy*

Initials of counsellor: _____

Date completed: __ __ /__ __ __ / __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __ /__ __ __ / __ __ __ __ Signed measurement nurse: _____

Initials of counsellor: _____

Appendix H

MCH-ART: Family Planning/Pregnancy intentions Phase 2 1st visit PID: 2 - __ __ __ __ - __ __
Xhosa-English Version 2.2, 27 Jan 2013

Family Planning and Pregnancy Intentions		Visit Date: __ __/__ __ __/__ __ __ __
Siza kubuza imibuzo malunga nendlela zocwangciso ntsapho okhe wasisebenzisa: *We are now going to ask you some questions about your use of family planning methods in the past:*		
1.	Zeziphi iintlobo zocwangciso ntsapho owakhe wasisebenzisa apha ebomi? *What methods of family planning have you used in your life?* (Funda urhangqe konke okungqamene nawe) *Read and circle all that apply*	a. Azikho *None* b. Ipilisi eziselwayo *Oral contraceptive pill* c. Isitofu se-2('noristerat NET-en') *2-month injectable ('noristerat NET-en')* d. Isitofu se-3 ('depo,petogen') *3-month injectable ('depo, petogen')* e. Isivalo –mlomo wesibeleko (IUD) *Intra-uterine device* f. Isivalo nzala sabantu ababhinqileyo *Female sterilization* g. Isivalo nzala sabantu besikhomo *Male sterilization* h. Idyasi kamkhwenyana *Male condom* i. Idyasi kamkhwenyana (yabantu ababhinqileyo) *Female condom* j. Olunye uhlobo,cacisa _____ *Other method, specify*
2.	Kwinyanga ezi-12 phambi kolu mitho, ubusebenzisa oluphi uhlobo lokucwangciso ntsapho? *In the 12 months before this pregnancy, what methods of family planning did you use?* (Rhangqa konke okungqamene nawe) *Circle all that apply*	a. Ipilisi eziselwayo *Oral contraceptive pill* b. Isitofu se-2('noristerat NET-en') *2-month injectable ('noristerat NET-en')* c. Isitofu se-3 ('depo,petogen') *3-month injectable ('depo, petogen')* d. Isivalo –mlomo wesibeleko (IUD) *Intra-uterine device* e. Isivalo nzala sabantu ababhinqileyo *Female sterilization* f. Isivalo nzala sabantu besikhomo *Male sterilization* g. Idyasi kamkhwenyana *Male condom* h. Idyasi kamkhwenyana (yabantu ababhinqileyo) *Female condom* i. Olunye uhlobo,cacisa _____ *Other method, specify*
3.	Ingaba uceba ukusebenzisa ucwangciso ntsapho emva kokubeleka? *Are you planning to use any form of family planning after delivery?*	Hayi *No* = 0 → **Gqithela ku Q5** *SKIP to Q5* Ewe *Yes* = 1

Initials of counsellor: _____

4.	Ukuba ngu-Ewe loluphi uhlobo ocinga ukuba ungalusebenzisa? *If yes, what method you think you might use?* (Rhangqa konke okungqamene nawe) *Circle all that apply*	a. Ipilisi eziselwayo *Oral contraceptive pill* b. Isitofu se-2('noristerat NET-en') *2-month injectable ('noristerat NET-en')* c. Isitofu se-3 ('depo,petogen') *3-month injectable ('depo, petogen')* d. Isivalo –mlomo wesibeleko (IUD) *Intra-uterine device* e. Isivalo nzala sabantu ababhinqileyo *Female sterilization* f. Isivalo nzala sabantu besikhomo *Male sterilization* g. Idyasi kamkhwenyana *Male condom* h. Idyasi kamkhwenyana (yabantu ababhinqileyo) *Female condom* i. Olunye uhlobo,cacisa _____ *Other method, specify*
5.	Ukuba ngu Hayi, nika izizathu ezingenza ukuba ungalusebenzisa ucwangciso ntsapho? *If no, what are the reasons that you might not use a family planning method?*	Izizathu: *Reason*
6.	Kwezi nyanga zi-12 ukhe wabonisana neqabane lakho ngocwangciso ntsapho okanye ukukhulelwa? *In the last 12 months, have you discussed family planning or pregnancy with your partner?*	Hayi *No* = 0 Ewe *Yes* = 1
Siza kubuza ngenjongo zakho zokumitha kwilixa elizayo: *We are now going to ask about your future pregnancy intentions:*		
7.	Cinga ngendlela oziva ngayo ngoku. Yeyephi kwezintetha zilandelayo echaza bhetele ingcinga zakho ngokuba nomntwana kwixesha elizayo? *Think about how you feel right now. Which of the following statements best describes your own thinking about having a child in the future?*	Ndingafuna ukuba nomntwana kwithuba lenyanga ezi-12ezizayo = 1 *I may want to have a child in the next 12 months.* Ndingafuna ukuba nomntwana ngelinye ixesha ingezizo inyanga ezi-12 ezizayo = 2 *I may want to have a child sometime in the future but not in the next 12 months.* Ndigqibe ukuba andifuni ukuba nomntwana kwixesha elizayo = 3 *I have decided that I do not want to have a child in the future.* Andiqinisekanga ukuba ndiyamfuna okanye andimfuni umntwana kwixesha elizayo = 4 *I am unsure about whether or not I want to have a child in the future.* Okunye = 5,cacisa: _____ *Other = 5, specify*

Date completed: __ __ /__ __ __ / __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __ /__ __ __ / __ __ __ __ Signed measurement nurse: _____

Initials of counsellor: _____

Appendix I

MCH-ART: Maternal adherence Phase 1(women on ART)
X-E Version 1.0 13 May2013

PID: 1 - __ __ __ __ - __ __

This CRF is to be completed by women on ART only

		Visit Date: __ __/__ __ __/__ __ __ __
1.	Yintoni igama lamachiza owatyayo? *What are the names of the ARVs you are taking?*	
2.	Ukususela ukuqala kwakho ukutya amachiza, wawuke wawayeka na? *Since you first started taking ART, have you ever stopped?*	Hayi *No* –> SKIP to Q5 Ewe *Yes*
3.	Mangaphi amaxesha uyeka uphinde uqalele ukutya amachiza? *How many times have you stopped and restarted ART?*	Amaxesha: _____ *# times*
4.	Bekunini ukugqibela kwakho ukuqalela amachiza? *When did you restart ART the last time?*	Umhla:___ Inyanga:_____ Unyaka:_____ *Day Month Year*
5.	iART uzithatha kangaphi ngemini? *How many times a day do you take your ART pills?*	Amaxesha: _____ *# of times*
6.	Zingaphi ipilisi ozityayo ngexesha? *How many pills do you take each time?*	# lipilisi:_____ *# of pills*
7.	Mangaphi amachiza entsholongwane ohlukeneyo owatyayo? *How many different HIV medicines do you take?*	# amchiza:_____ *# of medicines*
8.	Oko waqala ukuwatya,ungazibeka kweliphi inqanaba lokutya ngendlela owawuyibonisiwe yokutya amachiza akho? *Since you started taking them, how would you rate how well you usually do taking your HIV medicines in the way you are supposed to?*	Kakubi kakhulu=1 *Very poor* Kakubi=2 *Poor* Ndiphakathi=3 *Fair* Kakuhle=4 *Good* Kakuhle kakhulu=5 *Very good* Kakuhle okugqithisileyo=6 *Excellent*
9.	Ngoku cinga ngentsuku ezi-30 ezidlulileyo.yeyiphi kwezi zilandelayo echaza eyona ndlela otya ngayo amachiza akho? *Now think about the last 30 days. How would you rate how well you did taking your HIV medicines?*	Kakubi kunakuqala=1 *Worse than usual* Kakuhle kunakuqala=2 *Better than usual* Kuyafana njengesiqhelo=3 *About the same as usual*
10.	Kwintsuku ezi-30 ezidlulileyo,zimini ezingaphi okhe walibala ukutya amchiza akho entsholongwana? *In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?*	Intsuku: _____ *(0-30)* *# of days*
11.	Kwezi ntsuku zi-30 zidlulileyo uwatye kakuhle kanjani amachiza akho entsholongwane njengohlobo omele ukuwatya ngalo? *In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?*	Kakubi kakhulu=1 *Very poor* Kakubi=2 *Poor* Ndiphakathi=3 *Fair* Kakuhle=4 *Good* Kakuhle kakhulu=5 *Very good* Kakuhle okugqithisileyo=6 *Excellent*

Initials of counsellor: ___

12.	Kwezi ntsuku zi-30 zidlulileyo,kukangaphi usitya amachiza akho entsholongwane ngendlela omele kuwatya ngayo? *In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?*	Zange=1 *Never* Kumbalwa=2 *Rarely* Ngamanye amaxesha=3 *Sometimes* Ngesiqhelo = 4 *Usually* Malunga lonke ixesha=5 *Almost always* Lonke ixesha=6 *Always*
13.	Kunzima kangakanani ukutya amachiza akho entsholongwana ngendlela omele kukuwatya ngayo? *How hard is it for you to take your HIV medicines in a way you are supposed to?*	Kunzima kakhulu kakhulu=1 *Extremely hard* Kunzima kakhulu=2 *Very hard* Kunzima nje=3 *Somewhat hard* Akunzimanga=4 *Not very hard* Akunzimanga kwaphela =5 *Not hard at all*
14.	Kwintsuku ezi-30 ezidlulileyo ,zeziphi izinto ezibangele ulibale, okanye ezenze kubenzima ukutya amachiza akho? *In the past 30 days which of the following things made you miss a pill or made it hard for you to take your pills?* Zifunde zonke.Urhangqe zonke ezikhe zakwehlele. *Read all. Circle as many as apply.*	a. Bendingekho ekhaya *Was away from home?* b. Zilahlekile *Lost your pills?* c. Bendixakekile ndisenza omnye umsebenzi *Was busy with other things?* d. Ndilibele *Simply forgot?* e. Bezininzi ipilisi ebekufuneka ndizitye *Had too many pills to take?* f. Bendifumana imiphumela *Was getting side effects?* g. Bendibaleka imiphumela okanye ndingaziva mnandi *Wanted to avoid side effects or were feeling bad?* h. Bendizinika ikhefu kwipilisi *Wanted to take a break from the pills?* i. Bendingafuni abanye bazi ukuba nditya ipilisi *Did not want others to notice you taking medication?* j. Kuye kwabakho utshintsho kwindlela endisebenza ngayo okanye ngendlela endiqhele *Had a change in daily routine or work schedule?* k. Bendicinga ukuba ipilisi ziyasebenza noba ezinye andizityanga *Thought that the pills would still work even if*

Initials of counsellor: ___

		a few were missed? l. Bendiba amachiza ayingozi *Felt the drugs were toxic/ harmful?* m. Bendilele ngexesha lokutya ipilisi *Slept through dose time?* n. Ndizive ndingaphilanga *Felt sick or ill?* o. Ziye zandongamela *Felt overwhelmed?* p. Ndive ndino xinezelelo *Felt depressed?*

Date completed: _ _ /_ _ _ / _ _ _ _ Signed counsellor completing CRF:_____

Date of QC: _ _ /_ _ _ / _ _ _ _ Signed Measurement Nurse: _____

Initials of counsellor: ___

Appendix J

UNIVERSITY OF CAPE TOWN

HUMAN RESEARCH ETHICS COMMITTEE
09 OCT 2014
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.10.2015
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	pp TUBurgess	Date Signed	10/10/2014

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	06 OCT 2014		
HREC REF Number	451/2012	Current Ethics Approval was granted until	30 OCT 2013
Protocol title	Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study		
Protocol number (if applicable)	N/A		
Are there any sub-studies linked to this study?	✓ YES		
If yes, could you please provide the HREC Ref's for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study.	Estimation of delivery dates using obstetric ultrasound in the MCH-ART study REC REF 194 2013 On-going approval until 15 April 2014		
Principal Investigator	A/Prof Landon Myer		
Department / Office Internal Mail Address	CIDER, School of Public Health and Family Medicine, Faculty of Health Sciences		

1.1 Does this protocol receive US Federal funding?	✓ Yes	☐ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval?	☐ Yes	✓ No
1.3 Has sponsorship of this study changed? If yes, please attach a revised summary of the budget.	☐ Yes	✓ No

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

III. Article Appendices

Appendix A

Psychometric Scale Cronbach's (alpha score bolded if greater than 0.7)			
Self-efficacy (How confident are you that you can stick to your medication schedule...) **(Alpha=0.93)**			
Question (Item total correlation)	Mean (SD)	Median	Alpha with item deleted
When your daily routine is disrupted (0.69)	5 (1)	Very Confident	**0.93**
When the side effects begin to interfere with your daily activities? (0.75)	5 (1)	Very Confident	**0.92**
On weekends? (0.79)	5 (0)	Very Confident	**0.92**
When you are busy? (0.80)	5 (1)	Very Confident	**0.92**
When you are tired? (0.86)	5 (0)	Very Confident	**0.92**
When you are down or depressed (0.85)	5 (0)	Very Confident	**0.92**
When you are feeling healthy? (0.82)	5 (0)	Very Confident	**0.92**
When you are feeling sick (0.63)	5 (1)	Very Confident	**0.93**
When you drink alcohol (0.62)	5 (1)	Very Confident	**0.94**
When you don't want to be reminded about HIV/AIDS (0.74)	5 (1)	Very Confident	**0.92**
When it means taking your medications in front of people who don't know you are HIV+ (0.63)	5 (1)	Very Confident	**0.93**
When you are feeling sick from your pregnancy (0.75)	5 (0)	Very Confident	**0.92**
When you are busy taking care of your baby? (0.87)	5 (0)	Very Confident	**0.92**
When you are breastfeeding your baby? (0.83)	5 (0)	Very Confident	**0.92**
When you are tired from waking up with your baby? (0.85)	5 (0)	Very Confident	**0.92**

Continued Psychometric Scale Cronbach's (alpha score bolded if greater than 0.7)			
Beliefs About Medication **(Alpha=0.80)**			
My health during my pregnancy depends on my medicines (0.66)	4 (1)	Agree	**0.78**
My baby's health depends on my medicines (0.68)	4 (1)	Agree	**0.78**
Having to take medicines during my pregnancy worries me (0.78)	2 (1)	Disagree	**0.75**
Having to take medicines while I am breastfeeding worries me (0.78)	2 (1)	Disagree	**0.75**
Without my medicines I will be unable to care for my baby (0.65)	4 (1)	Agree	**0.78**
I sometimes worry about the long-term effects of my medicines on my baby (0.68)	3 (1)	Agree	**0.81**
When I am breast feeding my medicines will protect my baby from HIV (0.64)	4 (1)	Agree	**0.78**
Maternal Adherence Composite Score **(Alpha=0.84)**			
Since you started taking them, how would you rate how well you usually do taking your HIV medicines in the way you are supposed to? (0.83)	5 (1)	Very Good	**0.80**
In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to? (0.90)	5 (1)	Very good	**0.75**
In the last 30 days how often did you take your HIV medicines in the way that you were supposed to? (0.86)	5 (1)	Almost Always	**0.80**
How hard is it for you to take your HIV medicines in a way you are supposed to? (0.72)	4 (1)	Not hard at all	**0.85**

Continued Psychometric Scale Cronbach's (alpha score bolded if greater than 0.7)			
London Measure of Unplanned Pregnancy **(Alpha=0.88)**			
Question (Item total correlation)	Mean (SD)	Median	Alpha with item deleted
In the month that I became pregnant... (0.37)	2 (1)	I/we always used contraception	**0.91**
In terms of becoming a mother (first time or again), I feel that my pregnancy happened at the... (0.87)	1 (1)	OK, but not quite the right time	**0.84**
Just before I became pregnant...(0.96)	1 (1)	I did not intend to become pregnant	**0.81**
Just before I became pregnant...(0.96)	1 (1)	I had mixed feelings about having a baby	**0.81**
Before I became pregnant... (0.91)	1 (1)	We never discussed having children together	**0.83**
Before you became pregnant, did you do anything to improve your health in preparation for pregnancy? (0.48)	0 (0)	No actions	**0.9**
HIV Treatment Knowledge (Alpha = 0.32)			
Question (Item Total Correlation)		Percentage correct (%)	Alpha with item missing
Antiretroviral medication aims to reduce or suppress the activity of the HIV virus in the body. (0.13)		True (100)	0.32
Taking antiretroviral medications on schedule helps keep the right amount of medicine in one's system. (0.36)		True (97)	0.28
Viral load measures the amount of HIV virus in the blood. (0.51)		True (87)	0.28
Sometimes lab results say that a person's viral load is "undetectable." This means that there is no virus left. (0.41)		False (87)	0.34
Taking antiretroviral therapy exactly as prescribed is likely to reduce viral load. (0.25)		True (99)	0.31
Taking antiretroviral therapy can reduce a child's risk of becoming HIV infected during pregnancy and delivery. (0.52)		True (95)	0.22
Taking antiretroviral therapy can reduce a child's risk of becoming HIV infected during breastfeeding. (0.55)		True (90)	0.21
If a person takes antiretroviral therapy and has a low viral load, they may be less likely to transmit the virus through having sex with an HIV-negative partner. (0.53)		True (26)	0.39

Continued Psychometric Scale Cronbach's (alpha score bolded if greater than 0.7)		
HIV/Aids Knowledge Inventory (Alpha = 0.40)		
Question (Item Total Correlation)	Percentage correct (%)	Alpha with item missing
Is HIV/AIDS spread by kissing? (0.30)	No (97)	0.38
Must a person have many partners to get HIV? (0.32)	No (88)	0.4
Can a pregnant woman give HIV/AIDS to her baby? (0.54)	Yes (68)	0.34
Is HIV the virus that causes AIDS? (0.45)	Yes (82)	0.37
Is there a cure for HIV/AIDS? (0.30)	No (90)	0.4
Are there any medications a woman can take to protect her baby from getting HIV/AIDS? (0.37)	Yes (93)	0.37
Can a woman give HIV/AIDS to her baby during breast feeding? (0.53)	Yes (33)	0.35
Does formula feeding reduce the risk of a baby getting HIV? (0.48)	Yes (29)	0.37
Do caesarian sections reduce the risk of a baby getting HIV? (0.39)	Yes (17)	0.39

Appendix B

Spearman's Rank Correlation Matrix of Study Adherence Measures

	Number of Missed Doses in the last 30 days	Rate adherence since initiation	Rate adherence in last 30 days	In the last 30 days, rate how good a job you did in taking your ARVs	How hard is it to take your medication as you are supposed to
Number of Missed Doses in the last 30 days	1				
Rate adherence since initiation	-0.24	1			
Rate adherence in last 30 days	-0.48	0.75	1		
In the last 30 days, rate how good a job you did in taking your ARVs	-0.46	0.56	0.67	1	
How hard is it to take your medication as you are supposed to	-0.23	0.43	0.52	0.55	1

The above table shows a correlation matrix between the self-reported measures of association used in this study. All of the correlations were statistically significant, despite the majority of them showing only weak to moderate correlations. The main outcome measure, number of missed doses in the last 30 days, was kept as a numerical variable for this particular analysis, with a range of 0 to 30 missed doses. It has a negative correlation with all of the other reported measures, meaning that as a participant reports missing each additional dose, their self-report in other areas gets worse. The strongest correlation was observed between the rating of adherence in the last 30 days and since initiation (0.75). This strong positive correlation provides a good idea of how adherence in the last 30 days relates to a person's adherence history, and how they are nested together despite the different time frames. This could mean that adherence changes little over time, or it could mean that how well a person recalls taking their medication is affected by how well they have been taking it recently.

IV. Journal Submission Guidelines

JAIDS: Journal of Acquired Immune Deficiency Syndromes

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SCOPE

JAIDS: Journal of Acquired Immune Deficiency Syndromes is a peer-reviewed, multidisciplinary journal directed to an audience of physicians and researchers. The journal publishes original work in the form of Original Articles, Implementation and Operational Research*, Rapid Communications, Critical Reviews, Brief Reports, and Letters to the Editor*. *JAIDS* does not publish case reports. (*published online only)

MANUSCRIPT SUBMISSION

A submitted manuscript must be an original contribution not previously published (except as an abstract or preliminary report), must not be under consideration for publication elsewhere, and, if accepted, must not be published elsewhere in similar form, in any language, without the consent of Lippincott Williams & Wilkins. Each person listed as an author is expected to have participated in the study to a significant extent. Although the editors and referees make every effort to ensure the validity of published manuscripts, the final responsibility rests with the authors, not with the journal, its editors, or the publisher.

All submissions will be rigorously peer-reviewed by members of the Editorial Board and by other specially qualified individuals as well. In the interests of rapid reviewing of contributions, only one of the Editors-in-Chief will, in general, make the final determination as to the acceptability of a submission, after collecting the referee's comments. Contributors may recommend specific names of reviewers from the Editorial Board, as well as other individuals they deem especially well qualified. However, the Editors-in-Chief will not be bound to follow such suggestions.

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Clinical Science

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Journal Article

1. Schambelan M, Benson CA, Carr A, et al. Management of metabolic complications associated with antiretroviral therapy for HIV-1 infection: recommendations of an International AIDS Society-USA panel. *J Acquir Immune Defic Syndr.* 2002;31:257–275.

Book Chapter

2. Wortmann RL, Bentzel CJ. Renal handling of uric acid. In: Massry SG, Glassock RJ, eds. *Massry and Glassock's Textbook of Nephrology*. Phiadelphia: Lippincott Williams & Wilkins, 2001;90–92.

Entire Book

3. Mandell GL, Mildvan D, eds. *Atlas of AIDS*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.

Software

4. Epi Info [computer program]. Version 6. Atlanta: Centers for Disease Control and Prevention, 1994.

Online Journals

5. Friedman SA. Preeclampsia: a review of the role of prostaglandins. *Obstet Gynecol* [serial online]. January 1988;71:22–37. Available from: BRS Information Technologies, McLean, VA. Accessed December 15, 1990.

Database

6. CANCERNET-PDQ [database online]. Bethesda, MD: National Cancer Institute, 1996. Updated March 29, 1996.

World Wide Web

7. Panel on Clinical Practices for the Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services and Henry J. Kaiser Foundation, January 28, 2000. Available at: http://www.hivatis.org/guidelines/AA599.pdf.

Paper Presented at a Conference

8. Koenig L, Ellerbrock T, Pratt-Palmire M, et al. Prospective predictors of medication adherence: a study of the first six months of highly active antiretroviral therapy (HAART) using electronic monitoring [WePeB5818]. Presented at: XIV International AIDS Conference; 2002; Barcelona.

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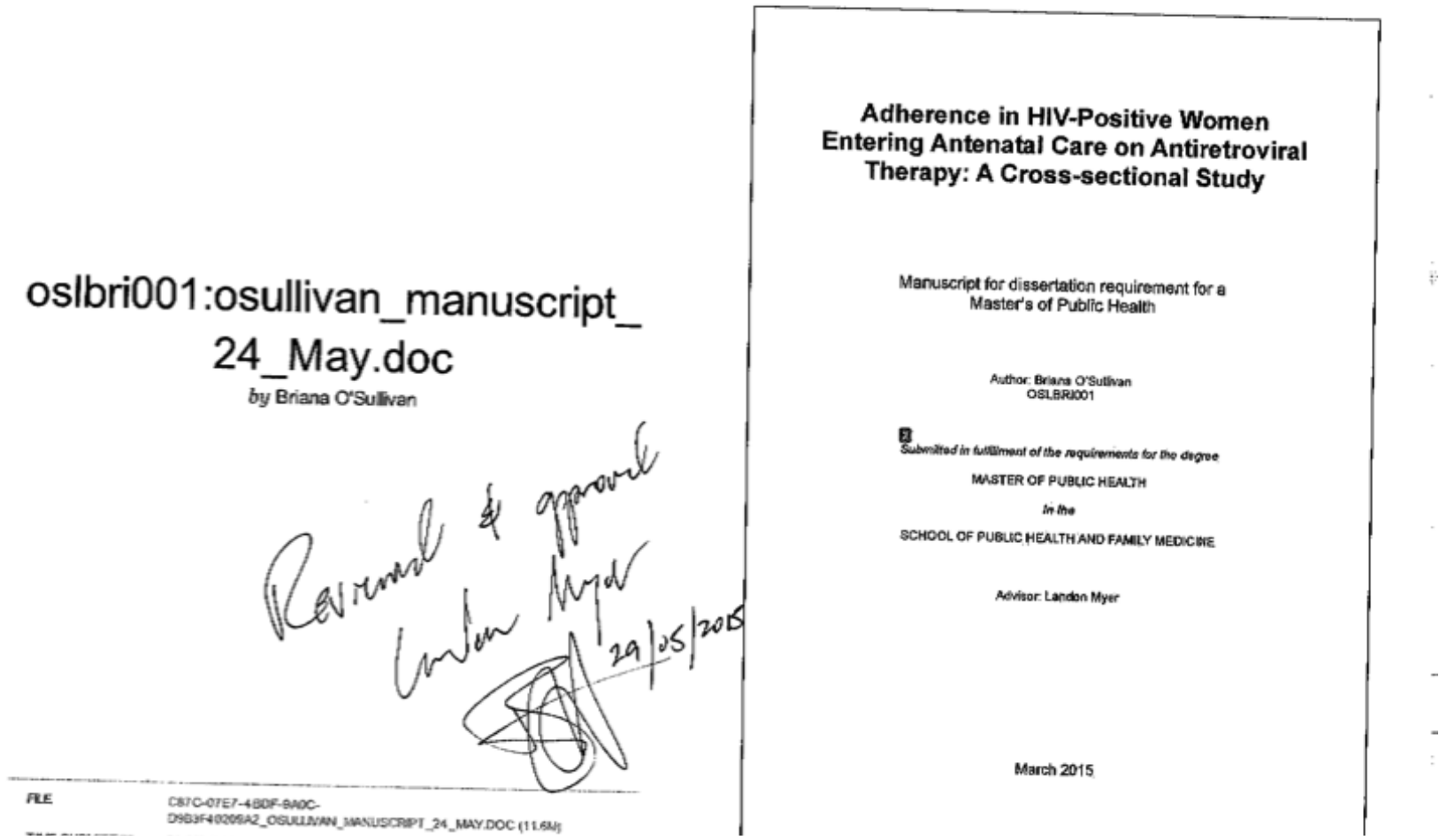

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Adherence in HIV-Positive Women Entering Antenatal Care on Antiretroviral Therapy: A Cross-sectional Study

Manuscript for dissertation requirement for a Master's of Public Health

Author: Briana O'Sullivan
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